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# ABSTRACT BOOK

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# 36TH ISCEV SYMPOSIUM

held at the Charles University - Faculty of Medicine
in
Hradec Králové, Czech Republic
June 13 - 17, 1998

# ABSTRACT BOOK

## THE RETINAL PIGMENT EPITHELIAL ELECTRICAL FUNCTION IN PATIENTS WITH MULTIPLE SMALL PIGMENT EPITHELIAL DETACHMENTS

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**Introduction:** Since the electrical function of the pigment epithelium (PE) may be severely impaired while only small fundoscopic alterations are visible, like in vitelliform dystrophy, we examined the PE by recording the electrooculogram (EOG) in a rare disease consisting of bilateral multiple small pigment epithelial detachments (PED) without age related macular changes.

**Methods:** Four healthy middle age with bilateral normal visual acuity, transparent ocular media in which fluorescein angiography revealed multiple PED in the posterior poles underwent EOG tests. After pupillary dilatation and light preadaptation, the EOG was recorded according to the standard protocol. The subjects seating in front of a full-field stimulator with silver disc fastened next to the canthin performed horizontal 30 degree alterating eye movements for 15 minutes in the dark, followed by 15 minutes in the light. The electrical potentials light peak/dark through amplitude ratio was calculated for each eye.

**Results:** The EOG lower normal value was considered 180%. In each examined eye the EOG determined ration was well above the lower normal limit indicating a normal functioning PE.

**Conclusions:** Our novel finding revealed in this rare retinal disease that despite multiple small PED the lesion seem to be confined to the affected areas while the overall electrical response is preserved.

# PROTECTIVE EFFECT OF DOCOSAHEXAENOIC ACID ON DAMAGED RETINA BY KAINIC ACID IN RAT

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**Introduction:** Docosahexaenoic acid (DHA) is highly enriched in the phospholipids of retinal photoreceptor outer segments, comprising up to one-half of the fatty acids of phosphatidylethanolamine and phosphatidylserine in rod-dominated retinas. A deficiency in DHA is associated with a loss of discriminant learning ability and visual acuity. The current study was designed to investigate the protective effect of DHA on damaged retina by kainic acid (KA) in rat.

**Methods:** Female Wistar rats aged 3 wks were used for this study. Following 14 days DHA dietary supplementation (1000mg/kg/day)( DHA group) and arabic gum solution in the same volume (control group), the right eyes of all rats were received intravitreal injection of KA in a dose of 3.12 nmol. An intensity series of ERG response was recorded on the 1, 7 and 14 days before and after KA injection. A cotton wick electrode placed on the cornea and a stainless steel needle electrode attached subcutaneously to the nasal bone as a reference. The amplitude and peak latency of the a- and b-wave and Oscillatory Potentials (OPs) were evaluated.

**Results:** ERGs after KA injection essentially showed a negative type, i.e. normal a-wave with greatly attenuated b-wave in both groups. However, the attenuation of b-wave in DHA treated rats group was lesser compared with controls. OPs were recordable in the DHA treated rats, while they were non-recordable in the control groups. The differences between DHA group and control group were progressively decreasing with time after KA injection.

**Conclusions:** The present results indicate that administration of DHA may prohibit the insult of glutamate neurotoxicity on the retina of rat.

## BINOCULAR SUMMATION OF VISUALLY EVOKED POTENTIALS IN NORMAL TENSION GLAUCOMA

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**Introduction:** To investigate binocular summation of visually evoked cortical potentials (VECP) in normal tension glaucoma (NTG).

**Methods:** Eleven normal control subjects and 11 NTG patients were examined. VECPs to monocular and binocular stimulation were recorded with pattern reversal and multifocal stimulation. Pattern reversal VECPs were recorded by varying check sizes at 20% contrast levels for 3 (transient VECP) and 12 (steady-state VECP) reversal frequencies. Multifocal VECPs were recorded with a use of Sutter's program. Amplitude and peak latency of the P1 component were estimated.

**Results:** No binocular summation effects were found in the normal control group. A spatial frequency characteristic curve was found it's maxima at 15 minutes of arc both in monocular and binocular stimulation records. In patients with NTG the curve based on peak latency and phase of pattern reversal VECP showed a significant depression at higher spatial frequency range for binocular stimulation, although no difference was found with amplitude measurements. Multifocal VECP showed no significant difference between normal controls and patients with NTG.

**Conclusions:** Our results were controversial to the past reports which showed binocular enhanced effects on pattern reversal VECP in normals. Based on our results in normals, we found high spatial frequency deficit for binocular stimulation in patient with NTG. It was, thus, suggested functional deficiency in binocular vision in NTG.

## OGUCHI DISEASE IN A GERMAN PATIENT DUE TO A HOMOZYGOUS 4-bp DELETION IN THE RHODOPSIN KINASE GENE

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**Introduction:** We describe the phenotype in the first patient diagnosed with Oguchi disease in Germany and a mutation in the gene encoding rhodopsin kinase (RHOK), and compare it with the phenotypes in (1) 3 unrelated patients with mutations in the same gene (Carr et al., Arch. Ophthalmol.73, 1965 and Carr et al, Invest. Ophthalmol. Vis. Sci.6, 1967) and (2) 8 patients from 6 families and a homozygous deletion (1147delA) in the arrestin gene (Nakazawa et al., Retina 17, 1997).

**Methods:** A 38 yrs old male was examined clinically including fundus photography in the light and dark adapted state. ERG was recorded according to the ISCEV Standard. Dark adaptation (DA) was tested with a short wavelength stimulus (500 nm cut-off filter, 64 mm2) 12° on the vertical below fixation until pre-bleach values were reached. Molecular results have been obtained as described earlier (Yamamoto et al., Nature Genet.15, 1997).

**Results:** The patient is the only child of unrelated parents. V.A. was 1.0 sc R.E. and 1.25 sc L.E. He was aware of problems with dark-adaptation since childhood. Funduscopy revealed a metallic-like reflex at the posterior pole o.u. that had vanished after 2.5 hours of dark adaptation. In the ERG the averaged rod-responses were non-recordable, the maximal-response of negative type with a low-normal a-wave and the OPs of low-normal amplitudes. Pre-bleach thresholds were reached after 2.5 hours of DA. SSCP analysis detected a homozygous 4-bp deletion in exon 7 in the RHOK gene: Ser536 (4-bp del) leading to a truncation of the C-terminus. Both parents were found to be heterozygous. The same mutation was previously reported in a compound heterozygote (Yamamoto et al., 1997).

**Conclusions:** The mutation in the RHOK gene in a German patient with Oguchi's disease confirms previous data on mutations in this gene to be frequent in patients of German origin compared to Asian patients with mutations in the arrestin gene (Fuchs et al., Nature Genet.10, 1995). The non-recordable averaged rod response, the negative maximal-response and the delayed dark adaptation are common functional features in patients with mutations in the arrestin and RHOK gene. Whereas cone responses were normal in patients with mutations in the RHOK gene, they had slightly reduced amplitudes in some patients with the arrestin 1147delA mutation. Further thorough electrophysiological and psychophysical examinations are needed in order to uncover the phenotypic differences in patients with mutations in the arrestin and RHOK gene.

**Acknowledgement:** Molecular genetic analysis was performed in Dr. Dryja's lab, Massachusetts Eye and Ear Infirmary, Harvard Medical School, 243 Charles Street, Boston, Massachusetts 02114-3096.

# MOTION-ONSET VEPS "AROUND THE CLOCK": BASELINE VALUES AND DIRECTIONAL TUNING OF MOTION ADAPTATION

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**Introduction:** The directional tuning of the motion-onset VEPs has not been systematically studied to date. We measured these potentials to motion in 8 directions around the full circle and obtained both baseline values and amplitudes after motion adaptation in one direction.

**Methods:** The stimuli were 10% contrast random dot patterns in a circular mask (dia 26°); when moving, then at a speed of 11°/s. Baseline blocks consisted of 2700 ms stationary pattern, 300 ms test motion sequences; adaptation blocks consisted of 2200 ms adapting motion to the right, 500 ms stationary pattern and 300 ms test motion. Eight test stimuli moving in 8 different directions in 45° steps were shown. Blockwise shuffling was employed to avoid sequential effects. In 11 subjects we recorded from occipital, occipito-temporal and central sites vs. linked ears. Eye movements were monitored with the EOG.

**Results:** Baseline amplitudes were around -4 microvolts and differed (non-significantly) by less than 15% between the eight directions. Adaptation reduced the N2-amplitude to 50% at all 7 non-adapting directions and down to 13% at the adapted direction. These effects were similar for all recording sites.

**Conclusions:** (1) Motion-onset VEPs are essentially symmetric "around the clock". (2) The marked adaptation in all non-adapting directions suggests that non-directional motion-evoked activity comprises about 50% of the response, while the remaining response arises mainly from direction-selective motion processing. Thus less than half of the motion response would reflect veridical motion processing.

This work was supported by the Deutsche Forschungsgemeinschaft.

## PATTERN ONSET AND REVERSAL VEPS FROM THE MULTI-FOCAL TECHNIQUE

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**Introduction:** The multi-focal technique, introduced by Sutter, offers the opportunity to record Visual Evoked Potentials (VEPs) from multiple small areas of the visual field. Thus, it opens the possibility to resolve some of the problems of the large-field VEP, caused by the heterogeneity of the stimulated area and the topography of its cortical representation.

**Methods:** The first step was to relate the kernel waveforms of the VEP obtained by this technique to the traditional pattern onset and pattern reversal VEP, and that was the aim of this study. We used an 8 x 8 checkerboard stimulus array (produced by EDI Inc), with each element of the array having the capability to contain from 1 to 16 checks, and containing, for this work, 4 x 4 checks. The contrast (first experiment) or the luminance (second experiment) was changed in a step-wise manner so that the stimulus was changed, in steps, from being pure pattern reversal to pure pattern onset. VEPs were recorded from a central electrode 2.5 cm above the inion, referred to a mid-frontal electrode, in response to each stimulus type (10 in all).

**Results:** Clear waveforms were produced in response to stimulation of the central four elements of the 8 x 8 array, particularly those in the lower half-field. Smaller responses were produced by stimulation of the more peripheral areas and these were lost in the noise in some subjects. For all stimulus types, responses were visible in the second order kernels only for pure pattern reversal, but were visible in both first and second-order kernels in all of the others, even though the overall luminance was perfectly balanced for the pure pattern onset stimulus.

**Conclusions:** These results suggest that pattern onset and reversal responses may reflect fundamentally different visual processes.

## MAPPING THE RETINAL FUNCTION IN PATIENTS WITH MACULAR HOLE USING A SCANNING LASER OPHTHALMOSCOPY (SLO) EVOKED AND MONITOR STIMULATED MULTIFOCAL ELECTRORETINOGRAM

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**Introduction:** To investigate central abnormalities in the retinal function in patients with macular hole using SLO evoked and monitor stimulated multifocal ERG.

**Methods:** 10 patients with macular hole (Gass II-IV) underwent SLO induced and monitor stimulated multifocal ERG (m-ERG) testing. On all patients an ophthalmic examination with a slitlamp and ophthalmoscope was performed. Afterwards patients underwent a fluorescein angiogram. The monitor stimulated multifocal ERG was performed as described by Sutter and Tran. In addition, a scanning laser ophthalmoscope was used as a stimulator and trigger unit. The stimulus matrix, containing of 19, 37 or 61 hexagones, is generated by a helium-neon laser. For simultaneous fundusscopy a infrared laser is used. The SLO unit (Rodenstock, München) is connected to a multifocal ERG device (Roland Consult, Wiesbaden). According to a pseudorandom m-sequence, the different hexagones of the stimulus matrix were stimulated concurrently, with the average luminance kept constant during the whole examination. Unless a pupil diameter is less than 3mm, dilatation of the pupil is not necessary.

**Results:** In contrast to the monitor stimulated m-ERG the SLO induced m-ERG allows a real time fundus control during the investigation, which enables the clinician to perform examination under simultaneous control of fixation. The hexagones which cover the local defects in the retina can be precisely correlated to the fundus picture gained by the SLO. The patients underwent SLO evoked and monitor stimulated multifocal ERG testing. The results were compared to the control subjects (40 eyes). In patients with macular hole, the amplitudes of the foveal region were reduced, whereas the extrafoveal parts of the retina showed a normal response. Also the latencies of the central retina were delayed, whereas in the exrafoveal retina normal latencies were observed. These results were seen in SLO evoked and monitor stimulated m-ERG recordings.

**Conclusions:** The SLO evoked m-ERG allows an objective evaluation of retinal function under control of fixation. In patients with macular hole a central reduction of amplitudes and a delay of latencies could be shown. According to the pathology of macular hole, which affects only the central part of the macula, no pathological answers were found in the extrafoveal parts of the posterior pole.

## ELECTIVE ENHANCEMENT OF THE PHOTOPIC ERG FOLLOWING EXPOSURE TO A BRIGHT RED BACKGROUND

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**Introduction:** We previously characterized (Rousseau et al., ARVO 1995) a New Photopic Light Adaptation Effect (type II LAE) as the transient enhancement of the photopic ERG resulting from an abrupt decrease in illumination from a brighter to a dimmer rod-desensitizing background (BG). The purpose of this study was to investigate the relative contribution of S-, M-, and L-wavelength sensitive cones to this effect.

**Methods:** ERGs were obtained from 5 normal subjects. Following a 5-minute exposure to a white light BG of 30 cd.m-2, control responses were evoked to flashes of white-light of 8 cd.m-2.sec. in energy. Subjects were then light adapted for another 5 minutes to a brighter (330 cd.m-2) BG of white- , blue- (460nm), green- (500nm), or red- (635nm) light. Following this, the luminance was returned to the dimmer control BG and a series of ERGs were obtained.

**Results:** ERGs obtained within the first 30 seconds following exposure to the brighter BG, show that our procedure did not significantly effect the a-wave, irrespective of BG used. In contrast, all b-wave amplitudes were enhanced ($p<0.05$), where the white BG produced an average 39% increase compared to 41% for red, 24% green, and 23% for blue. OP3 increased approximately 25%, regardless of background wavelength, while OP4 increased substantially with white-, red-, and blue-light BGs. For all chromatic backgrounds, OP2 was enhanced, with red-light showing the most dramatic increase.

**Conclusions:** Our results show that the type II LAE resulting from white light exposure can be replicated through cones that absorb light at long wavelengths. While blue- and green-wavelength sensitive cones might make a minor contribution to this effect, it appears that red-wavelength sensitive cones are solely responsible.

Supported by MRC grant 13383.

## CLINICAL AND ELECTROPHYSIOLOGICAL FINDINGS IN PATIENTS WITH CENTRAL SEROUS CHORIORETINOPATHY

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**Introduction:** The aim of the study was to estimate the prevalence of ophthalmological changes in patients with central serous chorioretinopathy, their character and course of the disease both in clinical examinations and electrophysiological investigations as well.

**Methods:** The full ophthalmological examinations and electrophysiological investigations were recorded in all 20 patients ( 2 females and 18 males, aged from 32 to 54 years, average age 39,5 years). The patients were devided into three groups: A) 3 patients with brand - new occurence, B) 11 patients within first three months of disease, and C) 6 patients with long duration and multiple recurrences. The investigations were repeated every three months in most of patients, during one year of observation. The diagnosis of the disease was confirmed in all patients by fluorescein angiography of the retina. The electrophysiological investigations were performed with Toennies Multiliner Vision equipment with Ganzweld stymulus for ERGs photopic, scotopic and oscillatory potentials and black-white checkboard used as the stimulus for VEPs . The ERGs and VEPs? analyses were based on three parameters -shape, latency and amplitude of components and compared to the results of the control group.

**Results:** The authors present a summary of relevant clinical and electrophysiological findings for each group of the patients. In clinical results the most frequent findings were: slightly reduced visual acuity, metamorphopsia, characteristical view in ophthalmoscopy and fluorescein angiography. The results of electrophysiological investigestions were normal in patients with short period of the disease (group A and B). In group C we observed reduction in amplitudes both in a-wave and b-wave and in oscillatory potentials.

**Conclusions:** In central serious chorioretinopathy the pathological changes are seen both in clinical examinations, fluorescein angiography and electrophysiological investigestions. Pathological results of the electroretinography depend on duration of the disease, extensivity of retinal changes and numbers of recurrences.

## MULTIFOCAL-ERG, PERG AND COLOUR VISION TESTING IN GLAUCOMA PATIENTS

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**Introduction:** In Germany, 2M patients suffer from glaucoma, and 40 K are blind. Early detection of patients with glaucoma helps prevent blindness if adequate treatment is applied. In addition to routine clinical methods colour vision are affected earlier than even computerised visual field tests. Sutter et al. reported that the second order Kernel may represent the function of the inner retina and the optic nerve head. Therefore we examined glaucoma patients with the M-ERG, PERG and Arden colour vision test.

**Methods:** a. M-ERG: 103 hexagons are presented on a 20 inch monochrome monitor driven at a rate of 60 Hz. Six cycles with a duration of 110 sec each were recorded. The luminance of the screen was 180 cd/m2 , the contrast nearly 98%. The m-ERG's were recorded with an contact-lens Jet-electrode. b. PERG: The PERG was recorded with 50 min of arc checks, presented at 2.2 Hz on a monochrome monitor with 16° diameter and 70 cd/m2. At least 100 responses were averaged and stored. The amplitudes of the P-50 and N-95 components were evaluated. The PERG was recorded with a gold foil electrode. c. Colour vision test: Colour vision was determined with the Arden colour vision test. Isoluminant letters lying either on the protan or tritan confusion line were presented in a binary search mode. (for details see Arden et al.,1988).

**Patients:** 25 patients with early glaucoma were examined. All patients with media opacities, systemic diseases and refractive errors > +/- 3 D. were excluded. None of the patients were treated with miotics. The patients received either betablockers or dorzolamid. None of the patients included in this study had severe visual field defects.

**Results :** The N-95 component of the PERG was significantly reduced in 12 of the patients. The other 13 patients had early glaucoma with so far no visual field defects and normal optic nerve head. Tritan colour vision defects were seen in 14 out 25 patients. In no patient was a protan defect observed. In 12 patients the 2nd. order Kernel was in the normal range. In all patients the amplitudes of the central hexagon as well as the first and second consecutive ring were in the normal range. However, in 13 patients the responses of the third and fourth ring were reduced in comparison to the normal subjects. A good correlation between colour vision, PERG and M-ERG was observed.

**Conclusions:** The m-ERG proved to be a helpful technique in controlling glaucoma patients.

## MULTIFOCAL ERG IN PATIENTS WITH X-LINKED JUVENILE RETINOSCHISIS

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**Introduction:** To investigate functional changes in x-linked juvenile retinoschisis by means of multifocal electroretinography.

**Methods:** Five young male patients with clinically defined x-linked juvenile retinoschisis were examined with the VERIS multifocal ERG system using a resolution of 61 elements within a 30° visual field. Peak amplitudes and implicit times of first order kernels were determined. Additionally, the b-a-ratio was analyzed and compared to Ganzfeld ERG Results:

**Results:** Central responses were reduced most, but all other responses within the stimulated area were also subnormal. Similarly, implicit times were delayed most in the center and somewhat less in the periphery. The typical signs in Ganzfeld ERG of delayed photopic responses and a reduced b-a-ratio were also found in the multifocal waveforms.

**Conclusions:** These results characterize the functionally affected region in patients with x linked juvenile retinoschisis. The area of amplitude reduction and implicit time delay was larger than the funduscopically visible defect. The maximal delay in the central area suggests that this region is most affected. However, all other eccentricities also showed subnormal results especially in implicit time indicating a more widespread defect.

## COMPARISON OF THE MULTIFOCAL-ERG-RECORDING-SYSTEMS VERIS AND RETISCAN

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**Introduction:** To compare the differences in handling and measuring techniques of the two Multifocal-ERG-Recording-Systems VERIS and Retiscan from a technical point of view.

**Methods:** By adapting the recording parameters of both systems as far as possible we generated comparable recording conditions and recorded multifocal ERG's of 15 normal probands aged between 20 and 36 years. The adaptation of the recording parameters included the illuminance and contrast-settings of the Stimulus-Monitor, amplifier-frequency-settings, recording time, stimulus pattern and timing and the use of the same electrode type (i.e. DTL and Burian-Allen).

**Results:** · There are huge differences concerning the capability of the Stimulus-Monitors used in terms of illuminance and contrast (maximum illuminance level of the Retiscan-System is about 78% of our normal VERIS-stimulation illuminance).

· Burian-Allen-Electrodes cannot be used with the available Retiscan-amplifier-configuration: The pre-amplifier has to be AC-based.

· Special-shielded electrode-cables and fine-tuned amplifiers used in the Retiscan system lead to a reduction of interferences of the electromagnetic environment. Thus it is possible to record ERG-data without using an additional line-frequency-filter at 50 Hz.

**Conclusions:** One major difference between the two systems lies in the illuminance and contrast settings of the Stimulus-Monitors used. The amplifiers used differ from each other significantly concerning the attenuation of electromagnetic noise. Additionally, the error-reduction-handling of the recorded data is completely different in both systems, which is also an indication that Retiscan is working as a linear system.

## FORMIC ACID ELEVATES THE C-WAVE AMPLITUDE AND DECREASES THE B-WAVE AMPLITUDE OF THE ELECTRORETINOGRAM OF THE ALBINO RABBIT EYE

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**Introduction:** Formic acid is the metabolite of methanol which causes toxic reactions in humans and nonhuman primates. Formic acid accumulates and leads to metabolic acidosis and serious visual impairment or blindness. These effects appear when formic acid has reached 8-15 mM concentration. In nonprimates, however, formic acid is oxidised to carbon dioxide and does not accumulate. Therefore, methanol administration causes only a certain central nervous system depression in these species.

**Methods:** The corneal direct current electroretinogram was recorded during simultaneous perfusion of the vitreous cavity of albino rabbit eyes with formic acid alternating with control solution.

**Results:** Perfusion with formic acid (10 mM) increased the c-wave amplitude significantly. This effect was reversible when the perfusion was changed back to the control solution after one hour. The a-wave was not significantly affected. The b-wave amplitude decreased somewhat during perfusion with 10 mM formic acid but this alteration did not reach statistical significance. However, when the perfusion was changed back to control solution, the b-wave amplitude increased significantly. With 50mM concentration of formic acid, there was a severe reduction of the b- and c-wave amplitudes and there was very little recovery after one hour perfusion of the vitreous cavity.

**Conclusions:** Formic acid affects mainly the b- and c-wave amplitudes of the electroretinogram of the albino rabbit eye. At lower concentrations the c-wave amplitude was elevated and the b-wave amplitude was somewhat decreased. The increase in c-wave amplitude may be caused either by an increase in the trans-pigment epithelial potential or by a reduction of the slow PIII from the Müller cells, or by both. The reduction in b-wave amplitude seems to indicate that formic acid is toxic mainly to the inner retina, presumably to the Müller cells. To further analyse the effect on the c-wave, intraretinal microelectrode experiments are in progress. Preliminary results show that the slow PIII is decreased while the trans-pigment epithelial potential is not affected. Thus, formic acid seems to have a direct effect on the Müller cells.

## ERG CHANGES IN PEDIATRIC EPILEPTIC PATIENTS FOLLOWING TREATMENT WITH VIGABATRIN WITHOUT ASSOCIATED VISUAL LOSS

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**Introduction:** Visual field loss has been reported in a minority of patients treated with Vigabatrin (VGB) for epilepsy (Elke et al., BMJ 314:181). VGB acts by elevating CNS GABA levels. The electroretinogram (ERG) is affected by elevated GABA levels in isolated retina (Gottlob et al, Vis Res 28:203). Our goal was to determine whether ERG changes following VGB administration are associated with changes in visual function.

**Methods:** 286 children (aged 2-16 yrs) with refractory seizures were enrolled in 2 double-blinded randomized clinical trials in which VGB or placebo was added on to the patients therapy regimen. Snellen visual acuity, Ishihara color plates, confrontation fields and ERGs (ISCEV standard protocol) were obtained during a pre-treatment baseline period and following 6 weeks of therapy.

**Results:** Blinded data indicated that in 36 of 140 patients with acceptable ERGs there were significant changes in the light-adapted response including a delay in the b-wave, reduction of b-wave amplitude, and marked reduction in oscillatory potentials. One of these patients had a change in visual field and one had a mild reduction in visual acuity from baseline. This rate of visual complication did not differ from that found in patients who did not show ERG changes or from that found in the total population.

**Conclusions:** Many patients treated with VGB have abnormal photopic ERGs. We find no evidence of increased incidence of visual dysfunction in these patients. The ERG changes are similar to those seen in isolated eyes perfused with GABA and probably represent normal physiologic effects of elevated retinal GABA.

## SLOWED RECOVERY KINETICS OF ROD AND CONE PHOTOTRANSDUCTION IN OGUCHI DISEASE DUE TO A NULL MUTATION IN THE RHODOPSIN KINASE GENE

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**Introduction:** Rhodopsin kinase (RK) is involved in quenching of light-induced signal transduction in photoreceptors. We investigated the effects on human vision of a mutation in the RK gene causing Oguchi's disease.

**Methods:** Fragments of the RK gene were amplified using PCR of genomic DNA. Wild-type and mutant RK were expressed in COS-7 cells and assayed for RK activity. The proband and his parent were studied clinically and with visual function tests including rod- and cone-isolated ERG photoresponses and rod and cone psychophysics.

**Results:** The proband had a homozygous deletion of exon 5 of the RK gene. In vitro experiments demonstrated that this mutation abolishes the enzymatic activity of RK and is likely a null mutant. Both homozygote and heterozygous parent had recovery phase abnormalities of rod-isolated photoresponses; photoactivation was normal. Kinetics of rod bleaching adaptation were dramatically slowed in the homozygote but normal final thresholds were attained. Light adaptation was normal at low backgrounds but became abnormal at higher backgrounds. A slight slowing of cone deactivation kinetics in the homozygote was detected. Cone bleaching adaptation and background adaptation were normal.

**Conclusions:** In this human in vivo condition without a functional RK reduction of photolyzed chromophore and regeneration processes with 11-cis-retinal probably constitute the sole pathway for recovery of rod sensitivity. The role of RK in rods would thus be to accelerate inactivation of activated rhodopsin molecules. Cones may rely mainly on regeneration for the inactivation of photolyzed visual pigment, but RK also contributes to cone recovery.

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## ELECTRORETINOGRAPHY AND PSYCHOPHYSICS IN CANCER ASSOCIATED RETINAL DEFICIT (CARD) SYNDROME

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Cancer associated retinopathy (CAR) is a rare, catastrophic condition which is marked by profound loss of function and retinal signals. However, we find that more subtle visual changes can be detected in many cancer patients. From 110 randomly-chosen volunteers with various neoplastic diseases, 13 have been tested to date and 11 report changes in visual function around the time of diagnosis and onset of treatment. In addition to routine clinical screening, measures were made of fields, color vision, dark adaptation and there were five types of photopic and scotopic electroretinal responses recorded. One of 26 eyes of cancer patients gave normal results on all tests. The clinical fundus examination was insensitive, with one eye showing pigmentary changes. One eye gave a Snellen acuity below 20/30. Among the psychophysical tests, Goldmann-type dark adaptation testing showed 25/26 eyes were abnormal. Among electrophysiological tests, supratheshold scotopic b-wave amplitude was least discriminating with 26/26 normal records. Most discriminating were photopic oscillatory potentials, where 15/26 RMS amplitudes were > 2 SD below the norm mean. Measures of cone-system function were generally more effected than those of rod systems. CARD is associated with many cancers or their treatment and produces quantifiable changes in large numbers of patients.

Assisted by Department of Ophthalmology and Research to Prevent Blindness.

If only the conservatives wanted to conserve and the liberals were in favor of liberty.

## STRUCTURAL AND FUNCTIONNAL EVIDENCE FOR A TEMPORAL WINDOW OF OXYGEN HYPERSENSITIVITY IN OXYGEN INDUCED RETINOPATHY (OIR)

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**Introduction:** As previously shown, newborn rats exposed to hyperoxia during the first 14 days of life exhibit dramatic and permanent changes in retinal structure and function, a condition known as OIR. The goal of this study was to investigate if we could demonstrate a window of oxygen hypersensitivity during those 14 days.

**Methods:** Litters of Sprague-Dawley rats were exposed daily to 80% O2, interrupted by 3x 0.5h of 21% O2. The first group of rats was exposed from birth to the 3rd, 6th, 9th, 12th and 14th day of life (i.e. intervals 0-3, 0-6, 0-9, 0-12, 0-14 days) and in the second group rats were exposed from the 3rd, 6th, 9th, and 12th to the 14th day of life (i.e. intervals 3-14, 6-14, 9-14, 12-14 days). Others groups were exposed between days 9-12, or from day 0 to 9 and day 12 to 14. Photopic and scotopic electroretinograms (ERGs) and oscillatory potentials (OPs) were obtained at 30 and 60 days of age. Retinal flat mounts and histology were also obtained at the above intervals. Rats which received the full treatment (0-14) showed a 70% decrease of ERGs amplitudes. The ERG data obtained for the other treatments were compared relative to the full treatment.

**Results:** Intervals 0-3 and 0-6 did not yield any significant ERGs alterations, while the 0-9 and 0-12 intervals resulted in 30% and 70% of maximal effect respectively. Similarly, the 3-14, 6-14 and 9-14 intervals produced 100%, 80% and 70% of maximal effect, while a 30% attenuation was observed with the 12-14 interval. Rats treated during the 9-12 interval yielded 30% of the maximal effect whereas those that combined the 0-9 and 12-14 intervals exhibited 40% of this effect. During the same intervals we observed a progressive reduction of all the OPs. At the maximum effect (0-14) OP2 was completely abolished, OP5 was reduced to 8%, while OP3 and OP4 were equally attenuated to 15% of normal. While present at all treatment intervals, the total amount of vasoconstriction and vasoobliteration obtained did not significantly differ between treatments. Histological analysis revealed that the retinas of rats exposed from 0-14 days failed to develop an outer plexiform layer. The same effect was observed for the 9-14 interval but not for the 0-9 one.

**Conclusions:** Our study suggests the existence of a critical period in OIR situated between the 9th and the 12th day since the exposures, which include this period, yielded major decline in ERG amplitudes, although a contribution of preceding and following periods must be considered. Our results also indicate that intraretinal damages more than the vascular changes are responsible for the functional anomalies reported. The differential effect of OIR on the OPs would also suggest that OP2, OP3-OP4 and OP5 are generated through three distinct retinal channels. MRC MT 13383

## ELECTROPHYSIOLOGICAL AND CLINICAL FINDINGS IN THE 172 PERIPHERIN/*RDS* MUTATION

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**Introduction:** The aim of this study was to characterise the phenotype of the 172 peripherin/*RDS* mutation.

**Methods:** 400 subjects with dominant macular and RP phenotypes were screened for peripherin/*RDS* mutations. Twelve families were identified with a 172 mutation. Nineteen representative patients underwent electrophysiological and psychophysical evaluation, including confocal scanning laser ophthalmoscopy (cSLO).

**Results:** Two mutations were identified: Arg172Trp in eleven families; Arg172Gln in the twelfth. Haplotype analysis demonstrated an ancestral relationship between all Arg172Trp families. Clinically, there was an age-dependent retinal degeneration confined to the macular region, usually presenting in the third decade. A typical granular appearance of the retinal pigment epithelium became apparent from early 20?s which developed into atrophic patches with increasing age, thence to larger areas of atrophy extending to the temporal superior and inferior arcades, and by the late 60?s becoming peripapillary. PERGs were affected early, and were often extinguished even with good preservation of acuity. All but one patient had normal EOG light rise and full field ERGs. There was high intrafamilial and interfamilial consistency. Autofluorescence on cSLO and PERG abnormality were shown to pre-date symptomatic presentation. One patient showed a different phenotype with a ?negative? Standard flash ERG, a delayed 30Hz flicker ERG and no EOG light rise.

**Conclusions:** The 172 peripherin/*RDS* mutation is usually associated with retinal degeneration confined to the macula. PERG abnormalities and autofluorescence on cSLO precede symptoms. Two different mutations showed markedly similar symptoms and signs.

## PHOTOPIC NEGATIVE RESPONSES IN THE FLASH ERG OF THE PRIMATE ARE REDUCED BY TTX AND BY EXPERIMENTAL GLAUCOMA EVEN WHEN FIELD LOSSES ARE SLIGHT

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**Introduction:** A photopic negative response (PhNR) peaking later than the b-wave of the macaque electroretinogram (ERG) is reduced in eyes with experimental glaucoma. We compared the development of these alterations in the PhNR with the progressive losses in visual sensitivity, and investigated the neuronal origin of the PhNR using pharmacological blockade of spiking activity of inner retinal neurons (ganglion and amacrine cells).

**Methods:** ERGs to brief (<6 ms) and longer (200 ms) red ganzfeld flashes of various intensities under photopic conditions (3.6 log scot td blue background) were recorded differentially between DTL fiber electrodes in the two eyes of 14 anesthetized macaque monkeys. Ocular hypertension (experimental glaucoma) was induced by argon laser lesions of the trabecular meshwork of one eye in each of ten monkeys. Visual field sensitivity was assessed by static perimetry using the Humphrey C24-2 full-threshold program. In four normal monkey eyes, tetrodotoxin (TTX: 3.8 microM) was injected intravitreally to block spiking activity of retinal neurons.

**Results:** ERGs, including the PhNR, were initially very similar in the two eyes of each animal. The PhNR peaked about 60 ms after a brief flash or 100 ms after the onset of a long flash. Following induction of experimental glaucoma in one eye, a- and b- waves remained unchanged even when the mean deviation (MD) over the visual field increased to -20 db. In contrast, experimental glaucoma greatly reduced the PhNR even when the MD was only -6db. As visual sensitivity continued to fall to lower levels than this, there was only a slight further reduction in the PhNR. Intravitreal TTX produced very much the same changes in the ERG as an experimental glaucoma involving a sensitivity loss of 6dB or more.

**Conclusions:** The results with TTX show that the PhNR of the macaque ERG depends upon the spiking activity of inner retinal neurons. However, the slow time course of the PhNR relative to the spiking response of ganglion cells raises the possibility that the response seen in the ERG is mediated by glial elements. Regardless of the mechanism of its generation, the PhNR, which also is present in the human ERG, holds promise for early non-invasive evaluation of retinal function in glaucomatous eyes.

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## PERSISTENT ROD DYSFUNCTION IN A RAT MODEL OF ROP

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**Introduction:** In a rat model of retinopathy of prematurity (ROP), test the hypotheses that 1) rod dysfunction persists in the mature retina and 2) the severity of dysfunction depends on the level of light in which the rats are reared.

**Methods:** Newborn albino rats were exposed to alternate high/low ambient oxygen until age 14 days. From 14 days onward, ROP rats and room air controls were reared in dim (2 lux) or bright (200 lux) cyclic light. As juveniles (30 days), and then again as adults (70 days), each rat had ERG studies of rod photoreceptor and postreceptoral function.

**Results:** Prior oxygen exposure and bright light cause significant attenuation of both the gain and saturated amplitude of the photoreceptor response. Furthermore, the interaction of oxygen exposure and bright light are significant. Age is not a significant factor.

**Conclusions:** In ROP rats, retinal dysfunction, primarily in the photoreceptors, persists in juvenile and mature rats reared in bright light. The dysfunction is similar to that observed in some children with resolved ROP. We suspect the retinopathy inducing and subsequent bright light exposures alter opsin expression and assembly of outer segment discs.

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## TO USE THE PATTERN REVERSAL STIMULATIONS TREAT THE CHILDHOOD AMBLYOPIA [ZHUWEI1]

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**Introduction:** to observe the effect of pattern reversal stimulation on childhood amblyopia with modified pattern reversal visual evoked potential(PRVEP)equipment.

**Methods:** the modified pattern reversal stimulation from Dantec Cantata 1500 ( H:W 3:1, contrast 0.75, reversal frequency 2Hz,1000 times once a day, 10 days for a period )was used respectively on OD/OS in 35 children with ametropic or anisometropic amblyopia between the ages of 5 and 8 years. In the mono-ocular amblyopia group, 11 amblyopic eyes and the controls with normal visual acuity were stimulated with reversal pattern. In the biocular amblyopia group,14 patients were stimulated with reversal pattern one eye after another,while in their control group 10 patients were stimulated with animated cartoon. Before and after treatment the pattern reversal VEPs were recorded from a single central scalp Ag-AgCl electrode 2 cm above the inion using the routine patterns.

**Results:** visual acuity and PRVEPs were significantly improved, the visual acuity was improved over 2 lines,the total effective rate was 78.6% in the biocular amblyopia group ,and 81.8% in the mono-ocular amblyopia group($P<0.01$); the latency of P100 from 112.5±12.72 ms to 101.72 ±5.86ms($P=0.0001$), the amplitude of P100 from 7.03 ±2.35 uv to 8.08 ±2.40uv ($P=0.0068$) in the biocular amblyopia group ;the latency from 108.91 ±8.41 ms to 101.4 ±9.92 ms ($P=0.0785$) ,the interocular difference of latency decreased from 7.60 ±4.53 to 5.90 ±3.93 ($P<0.01$),the amplitude increased from 6.34 ±2.63 uv to 7.58 ±2.25 uv in the mono-ocular amblyopia groups .No changes were found in the control groups with normal visual acuity or the amblyopic eyes stimulated with animated cartoon group.

**Conclusions:** the modified pattern reversal stimulation was effective in antiamblyopia according to the use of a physiological based functional biostimulation.Thus this method might be a new approach to treat yong childhood amblyopia.

**Keywords:** amblyopia, treatment, prvep, child

# FIS: A MULTISPECTRAL HARMONIC STIMULATION METHOD FOR THE ANALYSIS OF COLOR PROCESSING IN THE RETINA

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**Introduction:** In electrophysiology one needs an apropriate stimulus to measure the spectral sensitivity of an eye or of a single visual cell. Usually one uses monochromatic flashes, which have two disadvantages: First: It depends on the resolution how many single stimuli you have to apply to the system to cover a certain spectral range. Usually these stimuli start from dark to a certain intensity level. To keep the adaptational state of the eye stable you have to pause between the stimuli. Second: To compute a spectral sensitivity curve from the responses to these stimuli you also have to measure an additional intensity characteristics. Therefore a multispectral stimulation method called Fourier Interferometric Stimulation (FIS) was developed. With this stimulus linear and nonlinear components of the retinal reaction are simultaneously recorded and can be investigated, additionally a phase information is gained, which helps in analysing the processing of retinal signals. One can derive new information about the origin and the underlying retinal processes by comparing phase and amplitude spectra with other Results:

**Methods:** The output of a xenon lightsource is modulated in time and spectral composition by a continuously scanning Michelson interferometer. The output of the interferometer is called an interferogram. This stimulus will be presented at the poster site on a noteboook computer. This stimulus can be used in many different ways. Electrophysiologically the light will be projected in an Ullbricht sphere in front of the eye and the ERG-response will be recorded with an eye cup electrode. The stimulus- and the reaction-interferograms of the eye are Fourier transformed and scaled. The result will be a complex sensitivity of the whole eye, which reflects the processing of the retinal signals as will be shown in a seperate poster by F. Siebert, R. Gemperlein. One can also mix the output of the interferometer with white light and determine a psychophysical color sensitivity curve.

**Results up to now:** Using FIS a spectral sensitivity with a fine structure in the UV for the photoreceptor of the Blowfly Calliphora erythrocephala was detected. Electrophysiologically the Purkinje shift of the human eye could be measured. Psychophysically a colour contrast sensitivity curve of the human eye could be determined.

**Conclusions:** The FIS is a versatile stimulus. Using the FIS stimulus one can measure spectral properties in short time and high precision thanks to the advantages of Fourierspectroscopy, like high light throughput and simultaneous measurement of all spectral components. Analysing nonlinear reaction and phase one can determine color opponent mechanisms in the retina.

## MOTION VEPs WITH SIMULTANEOUS MEASUREMENT OF PERCEIVED VELOCITY

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The N200 amplitude of the motion VEP increases when the speed of an otherwise constant grating is enhanced. A positive slope of this function can be found at least for low speeds. For higher speed values the slope becomes shallower until saturation occurs. We asked whether the N200 amplitude is correlated with the perceived velocity in this range.

Gratings of vertical orientation, moving rightwards horizontally, were produced on a high resolution display having a frame rate of 100 Hz and an average luminance of 50 cd/m2. Reference and adaptation stimuli (spatial frequency = 2 c/deg) were presented parafoveally at an eccentricity between 0.5 and 3 deg left or right of the fixation point. The motion VEP of the reference stimulus was recorded from electrodes situated 10, 20, and 30 % left and right of Oz. The perceived velocity of the reference stimulus (speed = 2 deg/sec) was measured at the same time by speed comparison with a test stimulus presented in the other visual hemi-field (contrast of 4 %, spatial frequency of 1.2 c/deg, eccentricity of 3...7.2 deg). Individual maximum-likelihood estimates of the speed of the test grating which yielded 50 % "faster" judgment were determined by using a Best-PEST procedure according to Lieberman & Pentland.

Adaptation to stimuli drifting at 1, 2 or 4 deg/sec (contrast = 4 %) showed significant and nearly equal reduction of the N200 amplitude (Wilcoxon, p=0.05). The perceived speed, on the other hand, decreased after the fast adaptation condition whereas the perceived speed after the slow adaptation condition was significantly enhanced in comparison with the pre-adaptation judgment.

Our results can be explained by the channel hypothesis, i.e. neurons activated by a grating moving at 2 deg/sec contribute to the response level of either of two velocity channels, the "slow " or the "fast" channel. Whereas the motion VEP can only reflect the sum of both channel activities, simultaneous measurement of the perceived velocity can give additional information about the distribution of activity over both channels, and thus reduce the ambiguity in the motion VEP.

## SIMILARITIES AND DISSIMILARITIES BETWEEN PATTERN VEPs AND MOTION VEPs

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Pattern and motion VEPs can have a considerable similarity in their configuration. Stimulation with the same pattern could suggest the idea that the same neuronal population contributes to these potentials. The aim of this study is to explore the extent to which these potentials are affected by pattern or motion adaptation.

Pattern and motion VEPs were elicited sequentially by presenting subjects a stationary pattern for 1 sec, which is set into motion for another sec (speed = 2 deg/sec). The reference contrast of the gratings was varied between 0.5 and 64 %. The adaptation stimuli had a contrast of 4 %, a spatial frequency of 2 c/deg, and a speed of 0, 0.25, 1, 2, or 4 deg/sec. Adaptation and reference stimuli were situated in one of the visual hemi-fields at an eccentricity between 0.5 and 3 deg. EEG- electrodes were positioned 10, 20, and 30 % to the left and right of Oz.

Our results confirmed that pattern VEPs have a higher contrast threshold than motion VEPs. The amplitudes of the pattern VEPs, especially around 200 msec (N200), increased monotonically with increasing contrast up to 64 %. The final value was two- to fourfold the N200 amplitude of the motion VEPs. The latter was relatively independent of the stimulus contrast. The motion VEPs showed nearly equal N200 amplitudes in either hemisphere despite of visual hemi-field stimulation whereas the contralateral pattern VEPs exceeded the ipsilateral by a factor of 1.2 to 3.

Adaptation to stationary and to moving gratings reduced the N200 pattern VEP amplitude significantly (Wilcoxon, p=0.05). In contrast, the N200 motion VEP amplitudes remained constant after adaptation to stationary gratings, but diminished after adaptation to moving gratings.

The scalp distribution, contrast dependence, and adaptation effects support the view of an extensive independence of motion and pattern VEP generators. In addition, the experiments show that the extent of motion VEP amplitude reduction by moving grating adaptation is dependent on the contrast of the reference grating, with stronger reduction at lower contrast, in agreement with psychophysical Results:

## EFFECTS OF DIFFERENT CONCENTRATIONS OF DOPAMINE ON THE CORNEAL DIRECT-CURRENT ELECTRORETINOGRAM OF PIGMENTED RABBIT EYES DURING PROLONGED INTERMITTENT RECORDING

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**Introduction:** To investigate the long-term behavior of the pigmented rabbit d.c. ERG after intravitreal injection of dopamine of different concentrations.

**Methods:** The ERG was studied in 24 pigmented rabbits. Four experiments were performed, each including six animals. One eye was injected intravitreally with 0.1 ml dopamine (DA) with a estimated concentration in the vitreous body of 0.0025 mM, 0.025 mM, 0.25 mM and 2.5 mM, respectively. The contralateral eye was injected with the same amount of saline. Following the injection the animals were dark adapted for 30 minutes and then exposed to repeated light stimuli of low intensity for almost 3 hours (series I: 1 stimulus per 3 min, 10 s duration, light intensity 6.8 x 102 lux). After another 30 min period of dark adaptation repeated light stimuli of high intensity were presented to the eyes (series II: 1 stimulus per 70 s, 10 s duration, light intensity 6.8 x 104 lux) for 33 min.

**Results:** In the control eyes, a slow increase with time of the a-, b-and c-wave amplitudes was observed during series I. During serie II, the amplitudes were markedly reduced between the first and the second light stimulus, but subsequently attained a peak. The development of the ERG in the dopamine-injected eye with the lowest drug concentration was not different from that of the control eyes. At higher concentration levels the b-and c-wave amplitudes were reduced compared with the control eyes, and did not follow the slow increase with time observed in these eyes during series I. The peak observed during series II in the control eyes was increasingly suppressed in the eyes treated with dopamine.

**Conclusions:** When judged with the ERG, dopamine seems to influence the retinal adaptation process in rabbits in a dose dependent way.

## RECORDING A SINGLE ELECTRORETINOGRAM WITH SEPARATED CONE AND ROD COMPONENTS IN DYSLEXIA

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**Introduction:** Previous psychophysical studies report raised scotopic thresholds in dyslexia. This was attributed to a deficiency in docosahexaenoic acid (DHA). To further evaluate this we recorded simultaneous cone and rod electroretinograms (ERGs) in dyslexic subjects and controls.

**Methods:** Five dyslexics (mean 20.8 yrs, sd 3.1) were compared to age matched controls (mean 23.9 yrs, sd 4.3). All subjects were students from the same university. DTL fibres were inserted into the lower fornices and referenced to Ag/AgCl electrodes at the outer canthi, with vertex earth. After 30 minutes dark adaptation, monocular ERGs were recorded to square wave stimulation at 1.3 Hz. An improved separation of the responses was achieved by the introduction of longer wavelength light (a mixture of 700 and 660 nm LEDs illuminating a diffusing filter as a ganzfeld stimulus) and adjustment of the intensity of the stimulus (1.34 to 10.43 cdm-2).

**Results:** In controls, the ERG shows two eeonAE components (at 65 ms, sd 8 and 156 ms, sd 20), which have been attributed to the cones and rods respectively. A single eeoffAE component is seen at 523 ms (sd 15). At higher intensities, the cone component is larger than the rod. With decreasing intensity, the cone component decreases in amplitude until it is of a similar size to the rod component. Further decreases in intensity reduce the amplitude of both components. The rod and cone amplitudes may also be compared between subjects as a ratio, thus eliminating variations which may arise during recording, for example due to positioning of the DTL fibre . There is no significant difference in the latencies or absolute amplitudes of the cone, rod or off components, or in the cone:rod ratio, at any intensity for dyslexic and control subjects.

**Conclusions:** Separated cone and rod components in a single ERG are useful for comparing cone and rod activity and are applicable in many retinal pathologies. The use of a longer wavelength stimulus produces greatly improved responses. Dyslexics show no significant differences in amplitudes or latencies when compared with control subjects. This does not support the hypothesis of a retinal basis for raised psychophysical scotopic thresholds in dyslexia. Further investigations are currently being undertaken to consolidate these Results:

## RETINAL DETACHMENT - IS THERE A PLACE FOR ELECTROPHYSIOLOGY? I. PROGNOSIS FOR REATTACHMENT

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**Introduction:** Rhegmatogenous retinal detachment (RD) is still a one of the most serious sight-threatening retinal disorders, in which prognosis depends mainly on the duration and size of the disease. In order to find any objective prognostic factor of operative success (reattachment) in this study we correlated the electrophysiological data from patients with RD with their age, duration and size of the process in the context of result of the operation.

**Methods:** 32 patients with RD in the age of 26-76 (mean 55.2), 13 women and 19 men, with the duration of RD of 10-168 days (mean 42.8) undergone standard ERG (according to ISCEV standards), including scotopic, oscillatory potentials, L cone, B cone, fotopic and flicker. For statistical analysis (Spearman correlation) we used both results of the measurements (presented in mV and ms) (I) and results of the measurements calculated as the percent of the fellow eye (presented in % of the results of the fellow eye) (II). Pre- and postoperative status (degree of RD or reattachment) was presented in 4 and 5 degree scale respectively.

**Results:** No correlation between the age of patients, postoperative status (degree of reattachment) and studied ERG parameters (in both I and II) was found. However, we found that both L cone b wave implicit time and B cone b wave amplitude correlated with the duration of the RD ($r=0.81$ $p<0.02$ and $r=-0.70$ $p<0.05$ respectively) (II). We also observed correlation between the preoperative size of RD and several ERG parameters, i.e. scotopic a wave ($r=-0.54$ $p<0.002$), scotopic b wave ($r=-0.68$ $p< 0.00002$), fotopic a wave ($r=-0.71$ $p< 0.00001$), fotopic b wave ($r=-0.51$ $p< 0.005$), fotopic b wave implicit time ($r=0.71$ $p< 0.00001$), oscillatory potentials latency ($r=0.56$ $p< 0.002$), oscillatory potentials amplitude ($r=-0.51$ $p< 0.005$), flicker ($r=-0.76$ $p< 0.00005$) (II). Results for the I type of analysis were similar, although additional correlation was found between preoperative status, L cone a wave implicit time ($r= 0,79$ $p< 0.05$) and L cone b wave implicit time ($r=0.90$ $p< 0.001$).

**Conclusions:** Electrophysiologic parameters correlate with the preoperative size of RD, and thus may be used as the additional tool in RD diagnosis and treatment. However, the correlation between electrophysiologic parameters and postoperative effect was not found; the explanation of this is unclear. The correlation between duration of RD and two parameters obtained from colour stimuli need to be explored in detail in further studies since duration of RD is one of clinically used prognostic factors for reattachment.

## THE USE OF MAGNETOENCEPHALOGRAPHY IN STUDIES OF MOTION PERCEPTION IN PATIENTS WITH DISORDERS OF THE VISUAL CORTEX

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**Introduction:** We have previously reported on the use of magnetoencephalography in localisation and functional analysis of the human cortical area V5 ( Anderson et al 1996 ). Using our developed techniques we are able to locate dipoles within one gyrus with constricted MonteCarlo similated elipses. These locations can be co-registered with MRI. We have been able to study one patient demonstrating blind sight following severe damaged to the stribe cortex of one hemisphere. In addition we have studied a further patient whose lesion was thought to be immediately adjacent to area B5 both prior to and at surgery.

**Methods:** The Aston 20 channel magnetometer was used by being positioned over the visual cortex. The most stimulations consisted of iso luminent red green siusolent gratings in a horizontal configuration which drifted in a vertical direction. CO-registration with the individual patients MRI was obtained using a bite bar as we have previously described (Singh et al 1997). The visual stimulus be presented in any area of the visual field. For the study of the patient with blind sight stimuli would presented both 2.5 and 5 degrees out from the central fixation spot.

**Results:** Blind sight patient - When the stationery stimulus was presented to the patient either 2.5 or 5 degrees out in the blind hemifield no response could be obtained. When motion stimuli was presented clear responses were obtained in the blind hemisfiled of vision 5 degrees out and the response is localised at the gyros below the superior temporal fisher approximately to the human equivalent of V5. these results gave the same location as a pet study of the same patient. Presurgical Patient - The patient showed clear localisation of the motions centres to the same equivalent area as V5. The electrode quartography surgery confirmed these localisations and enabled the surgeon to remove unepileptic germ zone immediately adjacent to this area.

**Conclusions:** MEG provides accurate localisation of motion centres in the human visual cortex the advantage of the technique is that if necessary psycho physical studies can be performed purely based on the responsiveness of this area of the visual cortex.

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## MORPHOLOGY OF PATTERN ERG RECORDED WITH FULL FIELDS AND HALF FIELDS

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**Introduction:** The purpose of this study was to detect whether there are asymmetries in contrast generated retinal response which could be attributed to asymmetric structural and functional organization of nasal and temporal half of the retina.

**Methods:** Pattern ERG was recorded with full fields and half fields in 21 healthy subjects (12 male, 9 female, mean age 28.0, SD=2.65). PERGs were elicited by checkerboard pattern projected onto translucent screen of 16°r reversing at 1.6 Hz and recorded simultaneously from both eyes by HK-loop electrodes placed in lower conjunctival fornix. Responses were averaged and analysed by Nicolet MS 2000 system.To determine differences in morphology of the waves recorded from temporal and nasal fields, amplitudes of P50 and N95 waves were measured from the point that crosses the baseline between P50 and N95 waves (BL point).

**Results:** Measured from the BL point, mean value for full field P50 amplitude was 4.12 mV, and for N95 it was 3.44 mV. Mean latency for the baseline point between P50 and N95 was 78.36 ms. In half field responses, it was found that the amplitude of P50 measured from the baseline was larger from temporal half fields, i.e. nasal retinas (P50 temporal half field: 2.16 mV, nasal 1.81 mV) whilst the amplitude of N95 was larger from nasal half fields, i.e. temporal retinas (N 95 temporal half field: 1.71 mV, nasal 2.3 mV). There were also differences in latency of BL point, being 81.25 ms from temporal fields and 73.3 ms from nasal fields respectively.

**Conclusions:** There are clear differences in morphology of the PERG responses recorded separately from temporal and nasal retinas. Whilst stimulation of the nasal retina yields larger P50 and smaller N95, the reverse is true for temporal retina, where N95 predominates. This asymmetry suggests differential contribution to PERG waveform which should be carefully considered in interpretation of selective diminution of respective waves which was proposed as a diagnostic tool to differentiate between macular or optic nerve lesions.

## PATTERN ERG IN FOLLOW-UP OF RETINITIS PIGMENTOSA

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**Introduction:** We previously reported (ISCEV 1996), that PERG is better preserved than cone ERG in RP patients with good visual acuity. We further studied the responses obtained from the patients in different stages of the disease, to determine whether PERG could be used for follow-up when flash ERG responses are already absent.

**Methods:** ISCEV standard flash ERGs were recorded from 15 RP patients with various degrees of concentric field loss using Medilog OS2 Ganzfeld stimulator. Transient PERGs were elicited by 16°r checkerboard pattern reversing at 1.6 Hz. All responses were recorded by HK-loop electrodes placed in lower conjunctival fornix. Responses were averaged and analysed by Nicolet MS 2000 system. Results were compared with kinetic (Goldmann) and static (Octopus M1) perimetry, and visual acuity.

**Results:** Patients at advanced stage of RP with visual fields of less than 10° (II/4 mark) or mean defect (MD) of over 20 dB (Octopus M1) had absent both PERG and cone responses despite good visual acuity. In less severe affected patients, PERGs were still clearly preserved whilst the flash evoked responses were absent, despite the fact that they were elicited by a stimulus of much higher luminance than for PERG. This permitted follow-up by PERG which correlated well with deterioration of the visual field. On the other hand, PERG was not recordable from RP patients in whom visual acuity was poor (i.e. below 0.3) despite relatively preserved fields, or in patients with cone-rod dystrophy with relative central scotoma despite wide fields and preserved flash responses. Likewise, recordable PERG in RP patients was extinguished by applying a +3.0 diopter defocusing lens.

**Conclusions:** Good visual acuity is essential for PERG to be recordable in RP patients indicating that PERG is a contrast-generated retinal response which may reflect activity of the relatively preserved inner retinal layers. PERG may provide a useful electrophysiological tool for monitoring the retinal function in RP patients with good visual acuity in whom standard flash responses are already extinguished.

## CONE ELECTRORETINOGRAM IN RETINAL DETACHMENT

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**Introduction:** We investigated cone electroretinograms to white flash stimuli and to different color stimuli in eyes with retinal detachment.

**Methods:** 23 eyes of 23 patients, aged 17-71 years, with unilateral rhegmatogenous retinal detachment involving the macula were examined. Cone ERGs were recorded to Ganzfeld flash stimuli at 5 Hz in the presence of a bright white background illumination (50 cd/m2). Color flash stimuli were obtained by using Wratten color filters.

**Results:** The amplitude of the cone ERG b-wave, elicited by our brightest white flashes, was significantly correlated with the area of detached retina. Cone ERG b-wave implicit times to white stimuli were prolonged in most of detached eyes, compared with normal fellow eyes. The difference in implicit time was within 4 msec in cases with retinal detachment smaller than two quadrants. When the detachment covered more than half of the retina, however, the delay varied from 0-14.8 msec and did not correlated well with the area of detachment. In detached eyes, the short wavelength sensitive (S-) cone ERG, elicited by blue (450 nm) flashes, was more affected than the mixed long and middle wavelength (L,M-) cone ERG to red (633 nm) stimuli.

**Conclusions:** These results suggest that the non-detached retina may suffer from subclinical damages in eyes with larger retinal detachment.

## KINETICS AND SENSITIVITY OF MOUSE ROD FLASH RESPONSES DETERMINED BY PAIRED-FLASH ELECTRORETINOGRAPHY

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**Introduction:** A paired-flash ERG technique, in which a test flash delivered at time zero is followed at time t by a rod-saturating probe flash, has recently been used in human subjects to derive the approximate full time course of rod responses to weak test flashes (1). Previous studies of normal and transgenic mice have employed a similar paired-flash method to analyze rod recovery after bright test flashes (2-4). As the mouse is well-suited for studying genetically engineered changes in phototransduction reactions, it is of interest to develop the paired-flash method for investigations of normal vs. abnormal transduction processes in vivo. The present study of normal (C57BL/6J) mice was undertaken as an approach to this goal. Specific aims were to determine the flash sensitivity and time course of the ERG-derived rod response.

**Methods:** Dark-adapted C57BL/6J mice, 5-16 weeks of age, were anesthetized with ketamine/xylazine. ERG responses to full-field flashes were corneally recorded and amplified (bandpass of 0.1-3,000 Hz). Probe flash responses obtained in a series of paired-flash trials were analyzed for amplitude to yield A(t), the derived rod response to the test flash (1).

**Results:** The derived response A(t) obtained with weak test flashes exhibited a near-peak value at t = 80 ms. The dependence of A(80) on the test flash intensity If was described by the relation, A(80)/ADmo = 1 - exp(-k80 If), where ADmo is the dark-adapted maximal value of A(t) and where the sensitivity parameter k80 = 7.0 (scotopic cd-s-m-2)-1. For t > 40 ms, the weak-flash derived response was well described by an expression containing a delayed Gaussian activation term (5,6) and an exponential decay (7): $A(t)/ADmo = 1 - exp[-k80\ If\ g\ [1-exp(-a(t-td)2)][exp(-t/tw)]]$ where g = 1.78, td = 3.1 ms, tw = 160 ms, and a = 4.66x10-4 (ms)-2. However, the preceding equation overestimated, by about four-fold, the initial portion (t <15 ms) of the rod response (a-wave leading edge) determined in single-flash experiments.

**Conclusions:** The results provide in vivo information on the time course and sensitivity of phototransduction in the rods of normal mice. The kinetic data raise the possibility of a developing increase in transduction gain during the interval t »15-40 ms.

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## THE MULTI-CHANNEL VEPs TOPOGRAPHIES IN PATIENTS WITH LATE-STAGE GLAUCOMA

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**Introduction:** To study the clinical application of multi-channel VEPs topographies in patients suffering late-stage glaucoma.

**Methods:** The multi-channel VEPs topographies of 25 normal persons and 15 patients suffering late-stage glaucoma were recorded and analyzed. Humphrey perimetry was performed on all patients. The VEPs topographies were shown by computer proceeding of multi-channel VEP waves.

**Results:** In normal subjects, the topographies showed symmetric distribution by full-field pattern stimulation. In all patients with late-stage glaucoma, even whose visual field was severely damaged, multi-channel VEPs can be recorded, it showed irregular distribution simply "NPN" waveform, the reduced amplitudes of P1 waves and longer latency. The changes of topographies have observed.

**Conclusions:** The prognosis and evaluating treatment using multi-channel VEPs topographies is shown to be useful is late-stage glaucoma patients.

## BINOCULAR VISION OF MONOCULAR AMBLYOPES STUDIED WITH DICHOPTIC VEP

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**Introduction:** The binocular interaction was studied with transient VEP and steady-state VEP recorded with dichoptic checkboard reversal stimulation in 30 normal subjects and 22 cases with monocular amblyopia.

**Methods:** The dichoptic check-board stimulation were generated with a individual computer and a modulated haploscope. The binocular interaction was assessed as the binocular/monocular ratio (B/M) of the VEP amplitude.

**Results:** (1)In normal subjects, the amplitude of the binocular VEP is significantly reduced as comparing to that of the monocular VEP ,B/M ratio is 0.52±0.085.In patients, there was no significance variance in amplitude between the binocular VEP and the monocular VEP,B/M ratio is 8.9±0.112˚Ł (2)The difference in VEP amplitude to monocular stimulation of right and left eyes for both the normal subjects and the patients is not significant.(3)For the patients, the peak latency in the amblyopic eye is delayed 14±2.8ms than in the no-amblyopic eye,but there was no significant variance in VEP peak latency between the binocular VEP and the monocular VEP. Conclusions: there are binocular interaction in the visual system in the normal subjects, but for the binocular defects, the binocular interaction is lost or abnormal. Dichoptic VEP can be used to evaluate binocular function objectively.

**Key words:** binocular interaction, P-VEP, dichoptic stimulation, monocular amblyopia

# OBJECTIVE DETERMINATION OF INDIVIDUAL EQUILUMINANCE OF COLOURS BY VEP

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**Introduction:** Qualitative relationship between VEP-amplitude and the luminance of colours in checkerboard used was investigated. Based on these results an automatic adjustment of isoluminance control loop has been developed.

**Method:** For stimulation red-green, blue-yellow and grayscaled checkerboards containing 64 squares (1.7deg) were used. The temporal shape consisted of two different stimuli. The contrast stimulus was a reversal between two luminance levels of colours with a period of 166ms and a pulswidth of 1/2. The structure stimulus was a reversal between the colours with a period of 83ms and a pulswidth of 1/3. Special matrix of five electrodes was placed over the visual cortex to obtain maximal VEP-amplitudes. The different evoked responses were separated in the spectral domain. The contrast-correlated VEP was used to controll the luminance of colours to minimize its amplitude.

**Results:** The study of the relationship between VEP and the luminance was performed on 10 volunteers. In general, a minimum of contrast-VEP was expected at the individual equiluminance point. This behavior was validated in 4 cases with red-green and 5 cases with blue-yellow and gray squares. At the equiluminance point the VEP showed a maximum correlated with the structure stimulus in 6 cases with red-green, 7 cases with blue-yellow and 5 cases with gray squares. In the automatic evaluation mode up to 5 iteration steps were needed to attain the equiluminance point.

**Conclusions:** The study shows, that it is possible to evaluate the equiluminance point of an individual by automatic controll loop in an objective way. The examination time is relatively short (about 15 minutes), but not optimized. Up to date, only the absolute value of the contrast but not its sign at the equiluminance point can be evaluated.

## SHORT TERM ELECTRORETINOGRAPHICAL CHANGES FOLLOWING PANRETINAL ARGON LASER PHOTOCOAGULATION IN RABBIT'S RETINA

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**Introduction:** Panretinal photocoagulation is a well known, routine therapeutic procedure of several eye diseases. The character, the degree and the cause of development of the electroretinographical changes following the photocoagulation is not well cleared up. Our purpose was the recognition of the functional changes of the retina following panretinal photocoagulation with electrophysiological Methods:

**Methods:** 12 eyes of 6 rabbits were treated with indirect binocular laser ophthalmoscope: 6 right eyes with argon blue-green, 6 left eyes with argon green. We applied on an average 1200 laser burns per eye. Using different stimulation we measured the photopic and scotopic answers before, directly after, 1, 3, and 7 days and 1 month after the treatment. Results: Using the 0,25log SF stimulus we found significant decrease in the amplitudes directly after the laser treatment, which showed a similar pattern on the 1st and the 3rd day, but on the 7th day we observed an increasing tendency in the amplitudes. One month after the treatment the amplitudes were near to the pre-treatment values. Stimulating with standard flash we found quite similar tendencies, after the 7th day the amplitudes begun to rise. Under photopic conditions we observed a definite drop in the amplitudes as well, which showed a continuous increasing tendency. The implicit time values increased after treatment, their maximal values were measured generally on the 1st day, then they showed a slow regression. Considerable differences between the two eyes could be found only in the photopic a and b wave implicit time values, we found a smaller increase of implicit time in the eyes treated with argon green.

**Conclusions:** The electroretinographical changes (implicit time, amplitude) following the laser treatment showed an improving tendency from the 7th day. The above described electrophysiological changes can be explained by the damage of the blood-retina barrier due to the destructive treatment, which are nearly reversible after the pigmentation of the laser burns. It seems that argon green laser causes less photopic damage.

# RETINOTOPIC ANALYSIS OF ON-PATHWAY AND OFF-PATHWAY USING MULTI-FOCAL VEPS

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**Introduction:** To investigate the retinotopic distributions of On and Off-pathways , we compared the waveforms and the latencies of On and Off-responses of the Visual Evoked Potential (VEP) elicited from central and peripheral areas of the visual field by means of multi-focal technique.

**Methods:** Eight normal subjects took part in the study : 3 males and 5 females. We derived responses by using the VERIS II system and bio-amplifier. The stimulus was an array of 37 hexagonal elements, each independently alternating between black and white in pseudo-random achromatic stimulation (m-sequence=11). Each M-step comprised 20 frames and thus lasted for 266.67 msec. We divided 20 frames of M-step into On stimuli ( white ) and Off stimuli ( black ) and varied the duration of onset to give 6 timescales, 133.33msec, 106.66 msec, 79.99msec, 53.33msec, 26.66msec and 13.33msec. Inevitably as the duration of onset decreased shorter, the duration of offset increased longer. Total recording time was 8min. The active electrode was placed at 5% above Oz, referenced to the left ear lobe. The data were analyzed using VERIS Science 3.01 software. We compared between the average responses of the central elements out to 6.25 degrees (Group1); the next surrounding ring elements out to 12.5 degrees (Group2); the next ring elements out to 18.75 degrees (Group3) and the remaining ring elements out to 25.0 degrees (Group4).

**Results:** Both On and Off responses were observed in the1st-Kernel. The average latencies of the On-responses were, from Group1 to Group4 , 102.45 plus/minus 7.30 msec, 101.56 plus/minus 7.50 msec, 100.24 plus/minus 11.52 msec, 98.44 plus/minus 13.58 msec respectively. The corresponding values for the Off-responses were 120.80 plus/minus 6.88 msec, 121.08 plus/minus 8.34 msec, 116.86 plus/minus 10.36 msec and 114.30 plus/minus 12.32 msec. The average latency of Off-response was 17.59 msec greater than that of the On-response in each groups. The latency of On and Off response was shorter in Group4 than in Group1. The amplitude ratio of On / Off response were 3.99 plus/minus 5.19, 4.98 plus/minus 7.84, 2.47 plus/minus 3.05, 1.49 plus/minus 1.21 respectively. On the whole the amplitude ratio was largest in central area, decreasing towards the more peripheral areas.

**Conclusions:** The response in VEP of the On -pathway exhibit faster implicit time compared to that of the Off-pathway. The difference of the On / Off amplitude ratio between central and peripheral areas suggests a disproportionate distribution of On and Off dominant neurons from the retinal region.

## FLUORESCEIN-ERG. A SENSITIVE METHOD FOR THE DETECTION OF SUBCLINICAL VASCULAR DAMAGE IN IDDM PATIENTS

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**Introduction:** Ophthalmologists are generally discouraged from recording ERG during fluorescein angiography because of the possibility that the fluorescent substance may have a phototoxic effect on the retina. Recently, the advent of modern fluorescent materials that are entirely safe from phototoxic effect made possible the use of fluorescein-ERG. This presentation describes our findings with fluorescein-ERG in insulin-dependent-diabetes mellitus (IDDM) patients without any fluorescein leakage in FLAG examination.

**Methods:** Eleven patients (20-50 yrs of age, mean age 21 yrs) suffering from IDDM for 4-12 yrs were subjected to FLAG and repeated ERGs to investigate the effect of fluorescein. ERG was recorded before and five times during the 60 minutes interval after the injection. Thirteen eyes of good vision in volunteering patients with non-vascular damage of their fellow eye served as controls. ERGS were recorded with the help of gold foil electrodes. Responses to 50 flashes of blue light were averaged in each trial.

**Results:** In the control group there was a slight reduction in b wave amplitude immediately after fluorescein administration. We could not find any significant differences in ERG amplitude or latency values between the 0 min and 60 min recordings. In the IDDM group a considerable decrease than an intense rebound facilitation of the b wave was seen during the first 30 minutes. No complete recovery could be detected by the time of the 60 min recordings. Variance analysis showed significant differences between diabetic and control subjects in the time course of ERG amplitudes. No significant differences were found in the latency values. Significant differences were found between the diabetic values before and sixty minutes after fluorescein injection. No sign of any side-effects was detected.

**Conclusions:** Our study shows that ERG recording simultaneously with FLAG offers a rather sensitive diagnostic tool for detecting subclinical vascular damage in IDDM patients. The introduction of this diagnostic method in other vascular diseases of the eye is also recommended.

# INVESTIGATING COLOUR VISION DEFECTS USING TEMPORALLY EXTENDED STIMULI

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**Introduction:** It has long been recognised that colour vision defects may involve post receptoral abnormalities in addition to anomalies in the spectral absorption of the visual pigments. These anomalies cannot easily be elucidated by psychophysics alone, but can be investigated objectively by electroretinography. We report preliminary data on a series of subjects, varying from normality to cone monochromatism with excellent acuity, which has a prevalence of less than one in a million in the western population. Sustained stimulation is essential to isolate abnormalities of the off pathway and in this study two LED stimulators, one specially engineered and another commercially manufactured, were used to isolate the colour processing pathways.

**Method:** Nine colour defective subjects comprising four anomalous trichromats, four dichromats and one cone monochromat were compared with data from normal subjects. All subjects had good corrected visual acuity. ERGs were recorded with an interlocking square wave at 1.3 Hz and 30 Hz with 430, 525, 660 and 700 nm LEDs, and with 120 ms flashes at two second intervals with 450, 525 and 660 nm. Stimuli were applied over a diffusing field which closely approximated a Ganzfeld stimulus. To isolate responses from each cone pathway using three wavelengths, the active stimulus was applied intermittently in the presence of sustained background illumination consisting of the two complementary wavelengths, which were used to suppress the sensitivity of the remaining receptors including the rods. ERGs were recorded using DTL fibre electrodes with a Medelec Sapphire II 4E averaging system.

**Results:** In the normal subjects typical on and off responses for all three cones types are observed, with an attenuated off response in the case of the blue cone mechanism. Dichromats and anomalous trichromats produce characteristic waveforms with evidence of reduced sensitivity of L- or M-cone pathways. However in the case of the cone monochromat, relatively well formed responses were observed for S-, M- and L-cone types, however the off response of the L-cone appeared markedly attenuated.

**Conclusions:** The colour ERGs with intermittent stimulation with a rectangular temporal waveform and adapting complementary fields provided an objective test for comparison with conventional psychophysical data. Electroretinography allows investigation of both receptoral and post receptoral hypotheses in subjects with colour vision defects.

## BIETTI'S CRYSTALLINE DYSTROPHY

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**Introduction:** In 1937 Bietti described a tapetoretinal dystrophy (BCD) characterized by deposits of crystals in the retina and the marginal cornea. Only a few patients have been observed over a long-term period of up to 26 years.

**Methods:** We represent the clinical findings, fluorescein angiography (FLA), adaptometry and electrophysiology (ERG and EOG) of 2 patients (P1, P2). Findings of P1 have been documented over a period of 30 years, and Transmission electron microscopy (TEM) of peripheral circulating blood lymphocytes has been performed.

**Results:** A 21-year-old-man (P1) revealed tiny crystals scattered throughout the posterior pole of the retina. Three years ago problems in dark- and light adaptation were noticed. At age of 24, FLA demonstrated local atrophy of the RPE and ChC. Photophobia, nyctalopia, arcuate paracentral scotomas and constricted visual fields appeared during the 3rd to 4th decade indicating progression of the disease. Rod- and cone-driven responses (ERG) were subnormal and revealed a "negative ERG? in response to the sotopic maximal flash. The ratio of light- peak/dark-baseline (EOG) was reduced. During the 5th to 6th decade diffuse choroidal atrophy was evident, masking most of the crystalline deposits. Biomicroscopically, crystalline deposits were detected in the marginal cornea. TEM revealed crystalloid inclusions in lysosomes of lymphocytes. In contrast P2, presented these advanced findings of choroideremia-like appearance at age of 26 already.

**Conclusions:** Deposits of the retina associated with a reduced light rise (EOG) and impaired rod- and cone-driven responses (ERG) are important findings in BCD, especially in final stages of disease. The occurrence of deposits in the limbal cornea during the course of the disease and detection of crystalloid deposits in the lysosomes of lymphocytes confirm the diagnosis of BCD. They may help to distinguish BCD from chorioretinal dystrophies, e.g. choroideremia. In P1, the course of the disease is documented over the longest follow-up until now. P1 and P2 may at least in part represent two patterns of the manifestation of CDB.

## M-ERG RECORDED WITH A VGA-MONITOR OR SLO: A NORMATIVE STUDY

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**Introduction:** M-ERG proved to be a useful technique for examination of patients with retinal diseases. The first order Kernel represents the function of the outer retinal layers, while the second order Kernel is thought to exhibit the function of the inner retina and the optic nerve head. However, there are is no available normal data for various age groups. available.

**Methods:** VGA monitor: 103 hexagons are presented on a 20 inch monochrome monitor driven on a rate of 60 Hz. Six cycles with a duration of 110 sec each were recorded. The luminance of the screen was 180 cd/m2 , the contrast nearly 98%.

**SLO-system:** The SLO (Rodenstock, München) is the trigger and stimulus unit of the m-ERG (Roland Consult, Wiesbaden). The frame rate is 50 Hz. The stimulus is generated by a helium-neon laser (633 nm, 0-200 (mW). The retina and therefore the fixation is controlled by an infrared laser (780 nm, 0-2000 (mW). The stimulation field covers 14° of the posterior pole. 61 hexagons are tested. The m-ERG´s were recorded with an contact lens electrode (Jet) -electrode. The responses were analysed in regard to the absolute amplitude and latencies of each individual hexagon as well as for the central and the consecutive rings.

**Patients:** Patients were grouped into cohorts covering 6 decades, from 10-20, to 60-70 years. Six groups of patients in 10 years interval were examined from under 20 to over 60 years. Only patients with a normal ophthalmological status i.e. visual acuity equal or better 0.8 with an refraction not more than +/- 3 dpt., normal eye pressure and normal fundus were tested. All patients with systemic diseases such as diabetes, hypertonia etc. were excluded.

**Results:** The amplitudes of the second order Kernel were significantly smaller than for the first order Kernel. The amplitude ranged from 80 to 110 nV (mean 98 nV +/- 6.5 nV) for the central ring and 15 to 25 nV (mean 21 +/-2.4 nV) for the peripheral ring. The latencies of the central rings (mean 43 ms +/- 2.7 ms) are significant longer than for the peripheral rings (mean 35 ms +/- 2.6 ms). No significant difference between the age-groups 21 to 30 years and 51 to 60 years was observed.

**Conclusions:** We were able to demonstrate in a large group for normal subjects that the responses are highly reproducible and that the amplitudes for the second order Kernel are significantly smaller than for the first order Kernel.

## MULTIFOCAL ERG: EVALUATION OF RETINAL FUNCTION FOLLOWING MACULAR HOLE SURGERY

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**Introduction:** To evaluate development of retinal function following macular hole surgery.

**Methods:** In between May and December 1997 16 consecutive patients who underwent macular hole surgery (pars plana vitrectomy, peeling of the inner limiting membrane, thrombocyte concentrate application, intraocular gas tamponade) on one eye were examined with the multifocal ERG (VERIS Clinic II). Multifocal ERGs were recorded prior to treatment and 6 weeks after surgery. An additional examination at 4.5 months after surgery was performed in some of the patients. A stimulus pattern of 61 hexagons was used.

**Results:** Following surgery, in all 16 eyes the macular hole was closed. To compare multifocal ERGs the responses were summarized in rings as suggested in the VERIS software; ring 1 corresponds to the center of the stimulus, followed by rings 2-5 towards the periphery. In all eyes at all examinations detectable responses were present in rings 2 - 5. Prior to surgery in 5/16 eyes no definite response was detectable in ring 1. After surgery, detectable responses were recorded in 3 of these 5 eyes. In one of the other 2 eyes amlitudes increased in ring 2. In 11/16 detectable responses in ring 1 were present prior to surgery. Following surgery, increased amplitudes were seen in 5 eyes; amplitudes were unchanged in 3 eyes and were reduced in 3 eyes. Amplitude changes were evident 6 weeks after surgery without much change during further follow-up. Implicit times were unchanged in most cases following surgery.

**Conclusions:** Closure of macular holes was followed by improvement of multifocal ERG amplitudes in 9/16 eyes within 6 weeks after vitrectomy. Multifocal ERG amplitudes were unchanged in 3/16 eyes and deteriorated in 4/16 eyes.

## MOTION-EVOKED VEPs IN GLAUCOMA DIAGNOSIS

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**Introduction:** Motion perception as determined psychophysically can be disturbed in many glaucoma and glaucoma-suspect patients. In the present investigation, the usefulness of visual evoked potentials elicited by moving stimuli was investigated in glaucoma diagnosis.

**Methods:** Maxwellian-view system with an optical scanner. Retinal illumination 1000 Td, Stimulus duration 200ms, interstimulus interval 1800ms. Horizontal motion from right to left. Four different stimulus conditions were employed: 1.) Vertical square-wave stripe pattern (0.33 c/deg), low contrast of 0.04, field diameter 32°, velocity 10°/s. 2.) 0.88 c/deg pattern, contrast 0.04, field diameter 32°, velocity 5.9°/s. 3.) 0.88 c/deg pattern, high contrast of 0.93, field diameter 32°, velocity 5.9 °/s. 4.) 0.33 c/deg pattern, contrast 0.93, annulus field 23°-32°, velocity 10°/s. Recordings: Oz and P3 referenced to linked ear lobes. Amplification: 0.5Hz-70Hz, notch filter 50Hz. Sampling rate 250Hz, n=90. Evaluation of amplitude and peak time of N200 component. Testing of short-time reliabilty (2 measurements on the same day) and of long-time reliabilty (after 30 weeks). Three groups of subjects: 41 eyes of 34 normals (age range 21-72 years). 12 eyes of 12 pre-perimetric glaucoma patients (IOP > 21mmHg, papillometric defect, no perimetric defects). 28 eyes of 24 perimetric glaucoma patients (POAGs, SOAGs, LTGs, all with perimetric defects). Testing of validity by correlation analysis with perimetric MD value (Octopus 500).

**Results:** 1.) In normals N200 significantly larger at P3 than at Oz. 2.) Significant ($p<0.05$) negative correlation between N200 amplitude and age ($r=-0.377$) only under conditions 1 and 2 (low contrast), no significant gender differences. 3.) In perimetric glaucomas N200 at P3 significantly reduced under all 4 conditions, especially under conditions 1 and 4 ($p<0.0001$),peak times of N200 less significantly delayed under conditions 1 and 3. 4.) In pre-perimetric glaucomas non-significant trend of N200 reduction at P3 under all conditions tested. 5.) No significant differences in responses between Oz and P3 in perimetric glaucomas. 6.) Significant ($p<0.05$) negative correlation between N200 amplitude and perimetric MD ($r=-0.385$) only under condition 4 (annular stimulus). 7.) Good short-time reproducibility but poor long-time reproducibility of N200 amplitude at P3. 8.) Sensitivity 70% at specificity 80% under conditions 1 and 4.

**Conclusions:** 1.) Motion VEPs obtained from a parietal recording site serve as an additional valid test in perimetric glaucomas, especially when a low contrast or an eccentric stimulation is used. 2.) The test seems better suitable for cross-sectional analyses than for longitudinal analyses.

## VEP IN SMALL-FOR-GESTATIONAL-AGE INFANTS

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**Introduction:** Intrauterine growth retardation (IUGR) is one of the major problems in neonatal medicine. IUGR results in higher risk of morbidity and mortality. The children were born small-for-gestational-age (SGA), although genetically small children could not be excluded from the group. Earlier experimental studies in IUGR rats and sheeps have shown that the visual evoked potential (VEP) was abnormal with increased potential latencies and with altered VEP waveforms. Our intention was to investigate whether SGA-children have VEP-abnormalities as well. The criteria of selection was children of less than -2 SD regarding to weight with adjustment for gestational age. In 15 SGA-children ophthalmological examination, flash light VEP-recordings and clinical examinations were performed repeatedly from the first week of life to their first birthday.

**Results:** The results showed that there were altered VEP-forms in the SGA-children compared with the controls at six months of age and at one year of age. The latencies to peaks appearing in the VEP at approximately 100 ms after stimulis were prolonged, and the later part of the responses were less complex in its waveform compared to the normal VEP of healthy AGA-children (appropriate-for-gestational-age). With one exception the SGA-children appeared normal in the basic clinical examinations.

**Conclusions:** These results indicate that the visual function is changed in this group of children. The common clinical techniques for examinations could not reveal this impairment, probably because they are too insensitive. The VEP seems to be a promising method in identifying the infants at risk in IUGR.

# HOW MUCH INFORMATION IS NEEDED TO DETECT THE MOTION-ONSET VEP

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**Introduction:** To reveal useful information carried by motion-onset evoked potentials (M-VEPs) and to improve the EPs extraction, the time and frequency attributes of pre-stimulus EEG and M-VEPs were studied.

**Methods:** A group of five healthy volunteers was examined with linearly moving checkerboard (40'checks, 96% of contrast and mean luminance of 17 cd/sqm). To produce the typical N160 negative response, the following stimulus timing was used: the stationary pattern was presented for 3s, then moved at the velocity of 5deg/s for 600ms. We recorded twice 32 sweeps of 256 pre- and 256 post-stimulus samples with sampling frequency of 500 Hz from the leads Oz ,Or, Ol (5cm to the right (left) from Oz), Cz and Fz with A1 as the reference electrode. Data from pre- and post-stimulus parts of the M-VEPs were compared in frequency and time domain. We inspected changes in the power spectral density (PSD) and phase synchronization.

**Results:** 1. We found a strong phase synchronization to stimulus predominantly in the delta, theta and alpha band. 2. There was a high increase of PSD in the delta (90%) and theta (100%) bands and a slight increase of PSD (40) % in the alpha band of the post-stimulus interval. 3. We recorded a small decrease of post-stimulus PSD in the beta (18%) and gamma (10%) band. 4. In general, the post-stimulus PSD showed higher organisation (about 90% of variability was described by two independent components) when compared to the pre-stimulus PSD. 5. The diagnostic parameters (amplitude and latency of N160) obtained from the full M-VEPs frequency range were comparable with those estimated from delta and theta bands (1-8 Hz) only.

**Conclusions:** In healthy subjects, the evaluated M-VEPs components are generated mainly in theta and delta frequency bands. Reduction of the recorded frequency range can shorten recording time, decrease amount of data and improve "readability" of the M-VEPs. Specificity and sensitivity of the new M-VEPs parameters to the pathological processes remain to be evaluated.

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## MULTIFOCAL ERG IN PATIENTS WITH OPTIC NERVE DISEASES

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**Introduction:** The 1st order kernel of the multifocal ERG reflects a linear response to light and is comparable to Ganzfeld-flash ERG. The 2nd order kernel is a response to a change in local luminance and might therefore show similarities to the PERG. We tested whether changes patients with optic nerve diseases are observable in the linear and non-linear ERG components.

**Patients and Methods:** Patients with clinical defined optic nerve diseases (n=25) were examined with the multifocal ERG of Sutter & Tran (Vis Res 32: 433-446, 1992) and compared with a control group (n=30). The stimulus contains 61 hexagons in a 30 degree visual field. The first and second order kernels were calculated. Both were measured as peak-to-peak amplitudes.

**Results:** In normals, the 1st order kernel was lower in the nasal retina (2-11°) than in the temporal retina (ratio 0.8). The opposite was true for the 2nd order kernel (ratio 1.5). This can be interpreted as a sign for a relevant contribution to the 2nd order response generated near or at the optic disc. Astonishingly, the macular 2nd order activity was higher in the patient group than in normals (9.2 +/- 4.3 compared to 6.3 +/- 2.2 nV/sqdeg), while in the same region a normal 1st order kernel was measured (26.4 +/- 6.6 compared to 27.3 +/- 5.7 nV/sqdeg). The global averages of linear and nonlinear activity differed only to a minor degree (28.8 +/- 6.1 µV in patients to 29.9 +/- 6.8 µV in normal for the 1st order kernel. 8.7 +/- 2.0 µV in patients to 9.4 +/- 2.1 µV in normals).

**Conclusions:** The distribution of the 2nd order activity shows an asymmetry across the visual field with higher response densities in the vicinity of the optic nerve head. This indicate a ganglion cell contribution to the 2nd order kernel. The elevated high 2nd order responses in patients with optic atrophy may be explained by unmasking the retinal component by the loss of a ganglion cell component. The 2nd order kernel cannot simply be used as a local PERG for the detection of ganglion cell loss.

# MOTION-RELATED VEPS - REAPPRAISAL AFTER 10 YEARS' EXPERIENCE: I. METHODOLOGICAL ASPECTS

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**Introduction:** A routinely usable motion-related VEP technique was sought for with the aim of providing a method for better detection of magnocellular pathway disorders.

**Methods:** A large range of visual motion stimulation parameters (spatial frequency and contrast of the moving pattern; size of the stimulus and its location in the visual field; velocity, direction and duration of motion; interstimulus interval) was tested to specify their effect on the motion-onset/offset VEPs. An optical scanner system (moving mirror) and 21" PC monitor with 100 Hz picture frequency were used for visual stimulation. At the test distance of 0.6 m, the circular stimulus field subtended a visual angle of 30°. VEPs from standard bipolar occipital leads were compared with those from unipolar lateral temporo-occipital leads.

**Results and Discussion:** Motion-onset VEPs are determined to be the preferable for clinical use because of their larger amplitudes and lower inter- and intraindividual variability in comparison with motion-offset and motion-reversal VEPs (Kuba, M.and Kubová, Z.: Doc. Ophthalmol., 80, 1992, p. 83 - 89. Kuba, M. et al.: Physiol. Res., 41, 1992, p. 369-373.). The shape of the positive-negative-positive complex of motion-onset VEP peaks varied substantially under the influence of stimulus conditions, displaying dominant (or exclusive) negativity at about 160 ms (SD of 9 ms) for the following optimum motion stimulus parameters and recording conditions:

- temporal frequency (multiple of the spatial frequency and velocity) of 3 - 6 c/deg
- contrast of 5 - 20%
- stimulus field >= 15° (with macular masking in some subjects)
- random change of motion direction or simultaneous multidirectional motion ( e.g. expansion)
- ratio of motion duration/interstimulus interval (stationary pattern) >= 5 (preferred timing is 200 ms of motion and at least 1s of interstimulus interval)
- unipolar symmetrical lateral leads with electrodes located about 5 cm left and right from Oz position

Changes of these parameters can cause dominance of the first positive peak at around 120-130 ms which seems to represent a pattern-disappearance component. It may be caused by a blur effect in high temporal frequency moving patterns, by activity of the parvocellular system in high contrast patterns(Kubová, Z. et.al.: Vision Research, 35, 1995, p. 197 - 205.), by exclusive stimulation of central retina or by adaptation to unidirectional and too long and frequently repeated motion. Since both the pattern-related positivity and the motion-onset specific negativity appear simultaneously, the magnocellular pathway reactions should preferably be recorded from lateral occipito-temporal leads that best represent an activity of the MT areas. Discrepant findings in some laboratories are explicable by differences in the methods used, and by low number of subjects, since subjects can differ substantially in their sensitivity to single stimulus parameters.

**Conclusions:** On the basis of motion-onset VEPs recorded from about 200 normal subjects, a method has been developed which provides reliable information about magnocellular system function. These VEPs are recordable in about 95% of the human population.

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## Motion-related VEPs - reappraisal after 10 years' experience: II. Diagnostic applications

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**Introduction:** The previously-developed method for eliciting motion-onset VEPs (see previous abstract) was applied in the detection of magnocellular system involvement in various neuro-ophthalmological disorders.

**Methods:** In about 2,000 patients, latencies of the motion-onset specific negativity (N160) were measured (the upper limit of normal was 182 ms) in symmetrical lateral temporo-occipital leads, in addition to the standard pattern-reversal VEP recordings from Oz. Various moving stimuli, and repeat examinations, were used to estimate the clinical significance of motion-onset VEP findings.

**Results and Discussion:**

In patients with Multiple Sclerosis (without visual acuity reduction) it has been shown that demyelination can first selectively affect the magnocellular system (18% of delayed motion-onset VEPs accompanied by normal pattern-reversal latencies represent a substantial increase of the VEP examination sensitivity - Kubová, Z. et al.:Invest. Ophthalmol. Visual Sci., 35, 1995, p. 197.)

In Retrobulbar Neuritis, influencing mainly central fibres of the optic nerve, pattern-reversal VEPs which are always delayed, are less frequently accompanied by prolonged latency of the motion-onset VEP. This combination could be taken as a sign of demyeliniation.

Since the motion-onset VEPs are recordable to peripheral stimulation (up to about 40° from the fovea), they can be successfuly used for objective dynamic perimetry (Kuba, M. et al.: Vision Res. 35, Suppl., 1995, p. S166.) and for detection of early glaucomatous changes (Kubová, Z. et al.: Doc. Ophthalmol., 92, 1996, p. 211 - 221.)

Motion-onset VEPs do not display any distinct dependence on the visual acuity of subjects and they also seem to be unaffected by amblyopia (Kubová, Z. et al.: Vision Res., 36, 1996, p. 181 - 190.).Therefore they could be used for the testing of amblyopic eyes, when some additional neuro-ophthalmological disorder appears.

About 2/3 dyslexic children examined had prolonged motion-onset VEPs latencies, which supports the hypothesis of possible magnocellular system deficiency in some dyslexics (Kubová, Z. et al.: Physiol. Res., 44, 1995, p. 87 - 89.).

Motion-onset VEPs recorded from the secondary associate cortical sensory areas exhibit a higher sensitivity to subclinical encephalopathy and thus can be used in monitoring of CNS functions (Kuba, M. et al.: Acta Medica (Hradec Králové), 39, 1996, p. 21 - 26.).

**Conclusions:** The negative peak N160 of the motion-onset VEP provides new information on the functioning of the visual pathway. The clinical usefulness of this is clear. However, there remains a need for careful standardisation of numerous stimulus and recording parameters to avoid substantial differences between the laboratories.

**Acknowledgments:** This work was supported by the research grants from the Grant Agency of the Czech Republic (grant 309/96/0959), the Grant Agency of the Ministry of Health of the Czech Republic (grant 3230-3), by the European Community (CIPACT 930220 PL 924816) and by the James S. McDonnell Foundation for Cognitive Neuroscience, USA.

## STIMULI FOR THE MULTIFOCAL ERG USING THE RETISCAN

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**Introduction:** Adaptation the measuring system for the purpose of different multifocal examination tasks and the coupling with various stimulation devices.

**Methods:** The derivation of the multifocal ERG requires a device for representing the stimulus pattern usually consisting of a field of hexagons. The hexagons are controlled by shifted m-sequences. One step of each m-sequence consists of one ore more frames. The timing of the frames depends on the examination task and the characteristics of the stimulus device. There are differences in the timing between a CRT display and a laser scanning ophtalmoscope. Therefore it is necessary to adapt the controlling of the frames to different conditions.

**Results:** The adaptation of the measuring system offers the possibility for different multifocal examinations and the use of a CRT displays as well as a laser scanning ophtalmoscope for the stimulation display.

**Conclusions:** RETIscan is a measuring device for the multifocal ERG that is able to work with a CRT display as well as a laser scanning ophtalmoscope and to realise different multifocal examination tasks.

## HUMAN-LIKE PHOTOPIC ERGs IN GUINEA PIGS

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**Introduction:** We have previously reported (ARVO 1997) that the scotopic ERG of the adult Guinea Pig had a negative morphology which became more pronounced with flashes of brighter photopic range. In order to further characterize this unique feature, we investigated if this unusual morphology was readily present at birth. We also compared the physiological properties of the Guinea pig's ERG with that of human.

**Methods:** Photopic and scotopic intensity-response functions were obtained from light-adapted (background 30 cd.m-2) and darkadapted (up to 3 hours) Guinea Pigs (n=5) from day 1 to day 35 and compared to 4 adults ( > 7 months). The scotopic ERGs were evoked to flashes of white and blue light covering a 7.0 log-unit range in intensity (maximal flash luminance: 8 cd.m-2.sec). Photopic ERGs covered a range of 1.2 log-units. Human ERGs were recorded according to a standard protocol.

**Results:** At birth the scotopic a:b wave ratio is 1.2 ± 0.13, a value not different from the 1.14 ± 0.09 measured in the adult responses, indicating that the negative ERG morphology is already present at birth. With maturation however there is a progressive growth in the prominence of the OPs as seen on the ascending limb of the b-wave. Fast Fourier Transform analysis of the maturating ERG signal reveals that while the OP power content does not change with age, the frequency domain of the OPs increases from 105 ± 9 hz at birth to 125 ± 15 hz in the adult Guinea Pig. The latter maturation process similarly modified both photopic and scotopic responses. Interestingly, of all the animal species studied in this laboratory and elsewhere, we found that the adult photopic ERG response of the Guinea pig closely resembles that of the human. Like in human, at maximal intensity the photopic ERG is composed of three major OPs where OP2 has the lowest threshold and OP3 the highest. Similarly, in the Guinea pig the a-wave accounts for 40±6% of the suprathreshold photopic ERG amplitude compared to 33±4.4% in human subjects. The above combination produce, in the Guinea pig, a photopic ERG which is almost identical in amplitude, morphology, timing and frequency content to that of the human ERG. Also the different forms of light adaptation effects previously shown in human to be specific to distinct OPs also demonstrate the same specificity in the guinea pigs.

**Conclusions:** Our findings indicate that: 1- the unique morphology of the Guinea pigs bright flash scotopic ERGs results from an unusual and pronounced contribution of the OPs which is not readily present at birth; 2- the unique similarity between human and Guinea pig photopic ERGs (probably a consequence of similar proportion of cone photoreceptors) also suggests that the latter would represent an excellent animal model to study normal and abnormal human ERG function. Supported by MRC grant MT13383, FCAR.

## THE EFFECT OF DORZOLAMIDE ON THE ELECTRO-OCULOGRAM

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**Introduction:** carbonic anhydrase inhibitors have been shown to enhance the 'b' wave of the electro-oculogram both in humans and in experimental animals when injected intravenously. The mechanism of this effect is not known.

**Methods:** in this study the effect of the topical carbonic anhydrase inhibitor dorzolamide on the electro- oculogram was investigated. The EOG was measured in healthy volunteers after the application of either topical dorzolamide to one eye and saline to the other, or topical dorzolamide to one eye alone. At the time of testing the investigator was blind to which eye received the active drug. The same environmental conditions were present at each measurement. The effect of topical carbonic anhydrase inhibition on the EOG was evaluated by comparing the relative magnitude of the 'b' wave in the treated eye to the untreated eye.

**Results and conclusions:** no consistent effect on the standing corneo-retinal potential was found from topical dorzolamide. This suggests that the effect of carbonic anhydrase inhibitors on the EOG derives from an alteration to retinal activity. The clinical implications are discussed and the literature briefly reviewed.

## THE RETINAL EFFECT OF INTRAVITREAL INJECTION OF AMGIOSTATIC STEROIDS

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**Introduction:** Triamcinolone Acetonide was shown to be an effectiveangiostatic agent in cases of experimental PVR and ischemic retinaldiseases, such as branch retinal vein occlusion. In this work, we evaluatedpossible retinal toxicity by commercial Triamcinolone Acetonide (Kenalog)and two pure angiostatic drugs.

**Methods:** Three groups of Albino rabbits were studied for retinal effectsof Kenalog, Triamcinolone Acetonide (TA), and Tetrahydrocortisol-S (THC-S).Each group was treated by intravitreal injection of the experimental drugto one eye, while the second eye, serving as a control, was injected withsaline. The eyes of the rabbits were examined ophthalmoscopically. ERGrecordings were done before, 4 hours, 1 week, 2 weeks and one month afterinjection. At the end of the ERG follow-up period, the retinas wereprepared for histologic examination at the light microscopic level.

**Results:** Kenalog induced about 60% reduction in the amplitude of the ERGb-wave but had a negligible effect on the ERG a-wave. These effects wereevident as soon as 4 hours after injection and slightly increased withinthe next day. No recovery was seen for 30 days of follow-up. Histologicalobservations supported the ERG findings. Pure TA and pure THC-S, at a dosesimilar to that in the commercial drug and at a double dose proved nontoxic to the rabbit retina as assessed from the ERG responses and lightmicroscopy.

**Conclusions:** This work shows that Kenalog is retinotoxic, mainly to theinner retinal layers, and its experimental and clinical intravitreal useshould be avoided. On the other hand, pure TA and pure THC-S, are safe forexperimental use. These findings indicate that the toxic action of Kenalogis exerted by the preservatives in the commercial drug and not by theactive component.

## AGE DEPENDENCE OF MULTIFOCAL ERG AMPLITUDE AND IMPLICIT TIME

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**Introduction:** To assess the age dependence of peak amplitudes and implicit times of multifocal electroretinograms in normals.

**Methods:** 50 normal subjects aged 20-70 years were split into five groups, one per decade, with ten subjects each. Subjects were examined with the Visual Evoked Response Imaging System (VERIS) using a resolution of 61 hexagons within a 30° visual field. Peak amplitudes and implicit times of first order kernels were determined for all 61 elements, and medians and percentiles were calculated for each group separately. The Mann-Whitney test was used for the statistical evaluation of differences between groups.

**Results:** Although the study is not fully complete yet, our preliminary data from 41 subjects show that there is a loss of amplitude with age of about 1.1 μV per decade in the peripheral areas. In the center, amplitudes are dominated by interindividual variability, so that no good correlation with age was obtained. Implicit times increased with age at a rate of approximately 0.4 ms per decade in all areas. The typical "banana shape" of the implicit time distribution from center to periphery (all data: ring1: 32.3 ms, ring2: 30.2 ms, ring3: 29.8 ms, ring4: 30.2 ms, ring5: 30.9 ms) was present in all age groups.

**Conclusions:** Our data show that there is an age dependence of multifocal ERG Results: As expected, a reduction of amplitudes and an increase of implicit times were found in most regions. Although the multifocal ERG setups may differ between scientific groups, a similar age dependence can be expected. It is important to consider this dependence when patients or normals of different age groups are to be compared.

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## TREATMENT OF SECONDARY LASER-INDUCED DAMAGE IN THE RABBIT RETINA

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**Introduction:** We showed previously that laser treatment induced two typesof retinal damage; a direct one to the coagulated areas and a secondary oneto non-coagulated areas. The latter was attributed to development of serousretinal detachment between lesions. Our goal was to minimize the extent ofsecondary damage.

**Methods:** A fixed laser treatment (225 lesioned) was done in one eye ofpigmented rabbits. The other eye served for control. ERG responses weremeasured at different time intervals after laser treatment in order toassess functional retinal damage. Several treatments were tried in order tominimize secondary laser-induced retinal damage: hyperbaric oxygen alone;hyperbaric oxygen supplemented with injection of antioxidants andhyperbaric oxygen supplemented with injection of L-NAME in order to reducethe rate of nitric oxide formation.

**Results:** The ERG responses of laser treated eyes were reduced by about 50% immediately after treatment. Within 24 hrs, additional ERG reduction wasseen to about 90% of normal. Partial recovery was evident at 30 days afterlaser treatment. The time course and extent of ERG deterioration wascompared between the control rabbits (only laser treatment) and thoseundergoing potential therapeutic treatments. Hyperbaric oxygen treatmentalone did not affect the rate of ERG deterioration. Injecting a mixture ofcatalase and superoxide dismotase together with hyperbaric oxygen treatmenthad no ameliorating action. When L-NAME was injected together withhyperbaric oxygen, the degree of ERG deficit was smaller compared to thecontrol rabbits.

**Conclusions:** Secondary laser-induced damage to the rabbit retina can bereduced by a combination of hyperbaric oxygen treatment with injection ofL-NAME. It is hypothesized that L-NAME reduces the degree of retinaldetachment by constricting blood vessels and reducing edema while thehyperbaric oxygen treatment maintains adequate oxygenation of the retina.

# ASSESSMENT OF THE FOVEAL BIOELECTRICAL FUNCTION IN EYES OF PATIENTS WITH WET AGE-RELATED MACULAR DEGENERATION BEFORE AND AFTER ARGON LASER TREATMENT

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**Introduction:** The aim of this work was to determine whether Foveal cone ERGs (FCERGs) can be useful as a diagnostic tool in the evaluation of efficacy of argon laser treatment in eyes of patients with wet Age-related Macular Degeneration (AMD).

**Methods:** Foveal cone electroretinograms were recorded from 30 eyes with mean visual acuity 0.6 (Snellen Table) of 20 patients (mean age: 61 years) with wet AMD. The fovea was stimulated with a 5-degree flickering light spot (frequency: 31,25 Hz), surrounded by a 20-degree annulus of intensive, steady retinal illuminance. The stimulus was applied to the eye with the use of a hand-held stimulator-ophthalmoscope. FCERGs were recorded and analysed in amplitude according to the computer-aided method recently put in practice in our lab. FCERGs were obtained twice for each AMD patient: before and 3 months after argon laser treatment. The same procedure (FCERG recordings and analysis in two separate sessions) was performed in control group of 10 normal volunteers (10 eyes) of comparable age, in order to estimate FCERG amplitude differences (mean, SD) between two successive examinations. In the group of patients with wet AMD, the results were compared with normal FCERG values obtained in our lab (in this age group they were: mean amplitude = 0.22 mV, SD = 0.06 mV). Electrophysiological data were also compared with results of fluorescein angiography, visual acuity and visual field examinations (standard static perimetry).

**Results:** In the control group, the difference of FCERG amplitude between two examinations in sequence was not statisticaly significant (Student's t-test, p0.05). In this group Mean Difference = -0.048 mV, SD = 0.08 mV. We accepted normal range of FCERG amplitude difference between two examinations as Mean +/- 1.65 SD. In the group of patients with wet AMD, significant increase of FCERG amplitude after laser treatment was obtained in 33 % of analysed eyes. Significant decrease of FCERG amplitude was obtained only in two eyes (6%). In the remaining eyes with wet AMD, we did not observe significant changes in FCERG amplitude before and after argon laser treatment.

**Conclusions:** These findings suggest that Foveal cone ERG can be an useful test for objective evaluation of efficacy of argon laser treatment in patients with wet AMD. This test probably indicates patients with better prognosis.

## EVALUATION OF A NEW STIMULATOR FOR FOCAL ERG TESTING

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**Introduction:** We have evaluated a new focal stimulator (FCS-500, LKC Technologies, Inc.) for testing the macular retina. The stimulator uses a monocular indirect ophthalmoscope to present a 5 degree xenon (white) stimulus flickering at 31.25 Hz in a 20 degree background field.

**Methods:** Focal ERG's were measured in 47 eyes of 32 subjects with clinically normal macular areas. 24 eyes of 13 patients with various disorders of the macular retina were also tested. 38 Eyes of 21 patients diagnosed as having Retinitis Pigmentosa were tested as well. All patient's eyes were dilated. Testing was carried out with either Burian Allen bipolar electrodes or DTL electrodes. Focal ERGs were measured from the macular area of one or both eyes using the manufacturer's default protocol. Amplitude and timing parameters were extracted by Fourier Analysis.

**Results:** In 47 eyes with normal maculae, the focal ERG amplitude were 1239+/- 299 nV(Mean+/- S.D.). In 41 eyes with normal maculae using Burian Allen electrodes, the focal ERG amplitudes were 1260+/- 286 nV. In 6 eyes with normal maculae using DTL electrodes, the focal ERG amplitude was 1286+/-406 nV. For all eyes with normal maculae, the 95% lower limit of normal(LLN=Mean-2 S.D.) was 641 nV which is in good agreement with our clinical impression of an LLN of 700 nV. Normal implicit time was 34.4+/-1.7 msec.; the 95% normal range of implicit times was 31.0 msec to 37.8 msec. Focal ERG amplitudes in eyes with disorders of the macula were substantially lower than in normal eyes (359 +/- 228 nV). Patients with Retinitis Pigmentosa had Focal amplitudes that were also substantially lower than in normal eyes (344 +/- 222 nV).

**Conclusions:** The FCS-500 appears to be useful in the evaluation of retinal macular pathology.

## VISUAL EVOKED POTENTIALS FROM PAPER? PATTERN-ONSET CORTICAL RESPONSES TO A STATIONARY PATTERN

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**Introduction:** We wanted to demonstrate that the onset of fixation naturally occurring after a saccade is a visual stimulus comparable to pattern-onset, effectively evoking visual cortical responses (VECP) to a stationary pattern.

**Methods:** A 32' check-width, 10° stationary checkerboard was presented on the right half of an equiluminant uniform gray background, while a fixation cross was presented on the left half. The subjects alternatively fixated the cross and the checkerboard, while eye movements (EOG) and occipital cortical activity were recorded. The end of every saccade directed to the checkerboard (i.e. fixation-onset) triggered acquisition and averaging of occipital cortical activity. Conventional pattern-onset and pattern-reversal recordings have been obtained with the subjects fixating the same checkerboard modulated in time (100msec-ON 400msec-OFF and 4 reversal/sec, respectively).

**Results:** Cortical responses to fixation-onset were highly reproducible, and single traces were generally well defined without averaging. The waveform was almost identical to pattern-onset VECP and different from pattern-reversal. Decreasing contrast yielded attenuation and retardation similar in both fixation- and pattern-onset VECP. Notably a stationary pattern reproduced on paper was equally effective in evoking the "fixation-onset VECP".

**Conclusions:** A visual cortical response naturally occurs at the end of every saccade (EEG lambda waves) without need to temporally modulate the stimulus, and comparisons with the pattern reversal VECP have been already attempted with unsatisfactory Results: We demonstrate that the cortical response evoked by the fixation-onset occurring at saccade-offset actually is a pattern-onset VECP. This finding provides a better understanding of saccade-related VECPs as well as an effective way to study VECPs in a quasi-spontaneous condition from readily available stationary patterns (VECP from paper), and possibly from more complex images (VECP from anything?).

## ELECTRONYSTAGMOGRAPHY IN PERIODIC ALTERNATING NYSTAGMUS

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**Introduction:** Periodic alternating nistagmus (PAN) is a rare type of spontaneous nystagmus characterized by regularly recurring cycles; the shifting direction of the waveforms is caused by an actively shifting null zone. The cycles are of variable lenght, a compensatory movement of the head is often presents. In the cases studied at necropsy, multiple regions of the brain-stem have been involved (Towle and Romuald 1970, Towle 1971, Eane 1974).

**Materials and Methods:** We performed electronystagmography in five patients affected by congenital PAN and in one case affected by atypical periodic alternating nystagmus due to strabismus. VEP, ERG , opthalmological examination and RMN were also ruled out.

**Results:** The waveform of nystagmus was similar in four patients (jerk nystagmus), the leght of entire cycle was stable in each patient but was different each from other. In one case pendular nystagmus was superimposed. Atypical PAN showed absence of the slow movement of the head and lack of the null zone. This patient was esotropic and presented a regular period of the fixing eye. The direction of jerks reverted in dependence by fixating eye thus simulating PAN.

**Discussion.** Diagnosis of PAN must be suspected when electronystagmography is performed, particularly if anomalous position of the head is present. Differential diagnosis with atypical PAN must be done observing eye and head movements during electronystagmography. Electronystagmography with one eye patched could be useful in cases with strabismus.

## MULTIFOCAL ERG RESPONSES IN CENTRAL SEROUS CHORIORETINOPATHY

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**Introduction:** We have studied multifocal ERG responses after episodes of central serous chorioretinopathy (CSC), to compare affected and unaffected eyes.

**Methods:** We studied 4 patients (3 male, 1 female, ages 34-52) who had recent attacks of central CSC. The detachments were flat at the time of recording, but subfoveal fluid had been documented 1-7 weeks earlier. Multifocal ERGs were recorded from the patients, and from similar-aged normals, with VERIS (Tomey) instrumentation. Data were analyzed with software provided by Dr. E. Sutter, and were averaged from rings of retinal loci at different distances from the foveal center.

**Results:** Visual acuity in the affected eyes ranged from 20/15 to 20/40. The eyes with resolved serous fluid all showed a reduction in multifocal ERG amplitude (a- and b-waves) in the regions of prior detachment, relative to the fellow eye, and also a prolongation of b-wave time-to-peak. The a-wave times-to-peak were normal. The macular areas of fellow eyes showed ERG amplitudes that were suggestive of abnormality relative to normal subjects of similar age.

**Conclusions:** Focal ERG responses from areas of serous detachment did not return to normal immediately after fluid resolves, and showed reduced amplitude and b-wave latency delays relative to the fellow eye. Signals from the fellow eyes were suggestive of previous attacks or underlying diffuse choroidal pathology.

## A CASE OF UNILATERAL OFF-BIPOLAR CELL DYSFUNCTION

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**Introduction:** The objective of this study is to describe the electroretinographic and clinical findings in a patient with unilateral dysfunction of the retina.

**Case report and methods:** An 60-year-old woman was referred to us with a diagnosis of macular hole (stage 3) in the right eye. Vitrectomy sealed the macular hole, and the visual acuity improved from (0.2) to (0.9). Before surgery, single flash ERG was of "negative type" on the right eye and normal in the left. There was no complaint of night blindness or color vision abnormality. Because there was no other ocular fundus disease that could explain the ERG abnormality, she underwent additional psychophysical and electrophysiological examinations.

**Results:** Using a Ganzfeld stimulator, the cone (photopic ERG, 30Hz flicker) and rod responses were all decreased in the right eye compared with the left. The long duration stimulus revealed: 1) a waveform similar to the "depolarizing pattern"; 2) atypical rapid off-response composed by 4 to 5 oscillations peaks (not noise).

**Conclusions:** Selective blocking of the OFF-pathway with PDA or KYN resulted in depolarizing pattern, in animal models. Electrophysiological testings suggest that this patient revealed a retinal dysfunction with compromising of the OFF bipolar cells.

## ASSESMENT OF VISUAL POTENTIAL IN EYES WITH DENSE OPAQUE MEDIA

*Massoud W. H, El Din Gahal E., El Hamid A., El Hassan A., Genaidy M.M.*

**Methods:** In this work 30 eyes with dense cataract were studied. VER and ERG were perfomed preoperatively and visual acuity was assessed postoperatively.

**Results:** There was significant positive correlation between preoperative electrophysiological test results and visual acuity after surgery.

**Conclusions:** These results found basis for selection of cases of cataract suitable for surgery to get the best outcome. We recommend doing a preoperative electrophysiological studies for all cases of dense cataract undergoing surgery

## "TIME VARYING FILTERING" MAY REDUCE THE DURATION OF ELECTROPHYSIOLOGICAL RECORDINGS

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**Introduction:** "Time varying filtering" (TVF) is an analytical method (de Weerd 1981) to predict a noise-corrected ``true" response, whenever an estimate of the remaining noise in an electrophysiological response is available. We asked whether this method may shorten electrophysiological examinations under clinical recording conditions which are non-optimal for the proposed method, as the evoked potentials are usually modulated by varying attention and eye movement artefacts.

**Methods:** 12 subjects that visited our orthoptic department participated in the experiment. Their best corrected acuity was between 0.5 and 1.2, age ranged from 5 to 58 years. Transient VEPs (f = 1.7Hz) to two checkerboard stimuli with checksizes of 1.6 and 0.4 deg were recorded monocularly from both eyes. For each stimulus condition raw data of 200 trials were stored for offline analysis. Data analysis was performed in two steps. (1) For each condition an averaged VEP (``VEPa") of all trials was calculated. (2) The ensemble of trials was subdivided in subsets of (a) 4, (b) 10, (c) 20, (d) 40, or (e) 100 trials. Besides an averaged signal "S", a noise response "N" (by averaging with alternating sign) and a "true" signal S' (by TVF) were calculated for each subset. The mean-square deviation of S and S' from VEPa was averaged across all subsets for each analysis (a) to (e). This allowed to estimate how fast S and S' approximated VEPa when the number of trials was increased.

**Results:** For each analysis (a) to (e) the deviation of S' from VEPa was smaller than the deviation of S from VEPa. On average, the number of trials required for a specific approximation to VEPa could be reduced by a factor of 1.7 when TVF was applied.

**Conclusions:** The results suggest that TVF may reduce the duration of electrophysiological recordings significantly even under difficult recording conditions. Future studies will focus on the effect of TVF on amplitude and latency values.

# ELECTROPHYSIOLOGICAL TESTING OF ARTIFICIAL PHOTORECEPTOR DEVICES

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**Introduction:** To assess the function, biocompatibility and long-term stability of microphotodiodes, which had been implanted into the subretinal space of various animals.

**Methods:** Arrays of microphotodiodes (MPDA) designed to stimulate retinal neurons via integrated thin film electrodes had been implanted in the subretinal space in rats and rabbits. Ganzfeld-ERG, focal and multifocal ERG, and VEP have been used to examine the function of the host retina and the MPDA, as well as biocompatibility and long-term stability. Infrared stimuli allow the separation of the technical responses from the biological signal, as only the implants, but not the natural photoreceptors are sensitive to infrared light. Multifocal ERG technique combined with a scanning laser ophthalmoscope (SLO) allowed to exactly define the stimulated area of the fundus.

**Results:** 12 weeks after implantation the b-waves of rat eyes with implants showed a small reduction in amplitude, but no significant changes in latency compared with the partner eyes. The implants respond to light stimulation with large electrical impulses even 15 months after implantation. The SLO allows to image the fundus and the subretinal MPDA even in eyes as small as rat eyes. The position of the stimulating fields with respect to the retina and the MPDA can be clearly seen. First VEP results in rabbits reveal a small cortical response when the implant is stimulated with high intensity infrared light.

**Conclusions:** Electrophysiological methods are not limited to assess biological responses; they can furthermore be used to assess the function of artificial technical implants. Multifocal ERG can detect local currents at the site of the implants.

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## DEPOLARIZING PATTERN OF MACULAR CONE ERG (ON-MACULA) IN HUMAN MACULAR DYSTROPHY

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**Introduction:** In monkey, the depolarizing pattern of photopic long-flash ERG can be created by intravitreal injection of cis-2, 3-piperidine dicarboxylic acid (PDA). PDA blocks transmission at sign-preserving synapes from cones to hyperpolarizing bipolar and horizontal cells but leaves light-responses of depolarizing bipolars intact. The photopic long-flash ERG consists of a large positive b-wave with absent a- and d- (off) wave (Sieving PA et al, 1994). We found that some macular dystrophies show this pattern of ERG only in the macula.

**Methods:** Macular cone ERGs were recorded with 100 ms flashes and 15 deg spot size under the fundus monitor using infrared TV fundus camera.

**Results:** The waveform of macular cone ERG showed greatly prolonged b-wave with absent a- and d-wave. In some patients, the amplitude of b-wave was two times larger than normal and the ERG remained positive for the 100 ms flash duration. These ERG findings correspond well to the monkey ERG treated by PDA. The full-field ERGs were normal in photopic on and off components.

**Conclusions:** Some macular dystrophies may involve abnormalities in signaling by hyperpolarizing 2nd-order neurons rather than macular cones themselves.

## ELECTROPHYSIOLOGICAL STUDY OF RETINAL DETACHMENT

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**Introduction:** The electrical activity of the retina differs fron case to case post-operatively in retinal detachment. In this work the parameters wich influence the improvement or not of ERG after the operation are studied.

**Method:** Two hundred cases of different type of retinal detachment are studied in a follow up of 6 months post-operatively. ERG was recorded after 3' of full adaptation and Ganzfeld was utilized to produce photic stimuli. ERG was recorded preoperatively and one, three and six months after the operation.

**Results:** In the cases with a long standing retinal detachment the improvement of ERG after the operation is less than in those immediately operated. Also in young patients the improvement is higher than in the elderly people.The same occurs in cases of traumatic retinal detachment where the ERG post-operatively is better than in the idiopathic ones.

**Conclusions:** The post-operative electrical activity of the retina in retinal detachment surgery depends on many parameters, like the age of the patients, the early or late therapeutical approach of the disease and finally its etiology.

## SECOND ORDER KERNEL RESPONSE OF MULTIFOCAL ERG AND PATTERN ERG : APPLICATION TO PRIMARY OPEN ANGLE GLAUCOMA

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**Introduction :** Multifocal electroretinogram ( M-ERG ) and pattern ERG( P-ERG ) were recorded from the patients of early stage primary open angle glaucoma (POAG). All patients had unilateral glaucomatous visual field defect (i.e., stage II according to Kozaki's classification). First and second order kernel responses of M-ERG were compared with transient P-ERG responses.

**Methods :** 10 patients (20 eyes) diagnosed with early stage POAG, aged between 35 and 55 years old, were examined. Their corrected visual acuities were above 1.0 and no opacity was recognized for the optic media. M-ERGs were recorded using VERIS III system and a bipolar contact lens electrode, and analyzed by VERIS Science software program. P-ERGs were elicited using gold-foil electrode by the checkerboard pattern stimuli (38 min of arc check, 95% contrast, 3rev/s, 34.9cd/m2 mean luminance, 13.1 x 15.4 deg field). All the patients were examined by both Goldmann perimetry and Humphrey computed perimetry.

**Results :** P50 amplitude of P-ERG showed statistically significant difference in POAG between stage I and II, whereas other components (N95 amplitude, N35ĄP50ĄN95 latencies) didn't. No change that accorded with visual field defects was obtained from both first and second order kernel responses of M-ERG.

**Conclusion :** Second order kernel response of M-ERG was less useful than P-ERG P50 amplitude for understanding significant difference in the visual function of the early stage POAG.

# EFFECTS OF EXTERNAL NOISE ON CONTRAST THRESHOLDS IN NORMAL PATIENTS AND PATIENTS WITH EARLY GLAUCOMA: A COMPARISON OF BEHAVIORAL AND ELECTROPHYSIOLOGICAL THRESHOLDS

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**Introduction:** We tested the hypothesis that because of their reduced neural efficiency, glaucoma patients should have increasingly impaired thresholds as external noise is added to a stimulus.

**Method:** We compared the performance of 20 normals (mean = 39 years) with that of 1 5 patients with early glaucoma or at very high risk for glaucoma (mean = 45 years). All patients had visual acuity of 20/20 or better at the viewing distance of I meter. Contrast thresholds were measured on two sets of tasks: behavioral and contrast sweep VEPs. For both types of tasks two stimuli were used: 7.5 Hz reversing gratings of 0.7 cpd, and 5.5 cpd gratings. Noise was binary and contrast varied from 0 to 80%. Thresholds were determined using a staircase which employed a 4 AFC and converged on 50% correct. Sweep VEP thresholds were determined by extrapolation to Zero volts as a function of log contrast.

**Results:** In general, the differences between normal subjects and the patients with early glaucoma were not significant at 0 noise level conditions. Both the absolute size of the difference and its significance increased With increasing noise level. However, for the behavioral thresholds these trends were clearer with the 5.5 cpd grating; for the sweep VEPs they were more clear for the 0.7 cpd grating.

**Conclusions:** The performance deficit of glaucoma patients which may be minimal under normal testing conditions can be magnified when external noise is added to the stimulus. However, VEPs and psychophysical thresholds show differences in their sensitivity to this effect. Implications for the early detection of glaucoma will be discussed.

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## OSCILLATORY POTENTIALS OF THE ELECTRORETINOGRAM AS A TEST FOR RETINAL AUTOREGULATION

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**Introduction:** In a previous paper on a limited number of normal subjects, the AA showed amplitude reduction of the Oscillatory Potentials (OPs) of the flash Electroretinogram after application of an artificially induced ocular hypertension; on such basis, they speculated the possibility of investigating the retinal autoregulation by means of the OPs but the number of subjects did not any inference about that item. The AA present the data colected in a larger number of normal subjects and analyse the OP changes by comparing the reults obtained in selected pathologies.

**Methods:** The scotopic and photopic flash ERG were recorded in a group of 15 normal volunteers as the intraocular pressure artificially raised by means of the suction cup method from 0 to 40 mm Hg in steps of 10. The OPs were recorded in basal condition and after recovery as well. We took into account the changes of the amplitude and latency of each wavelet, both scotopic and photopic. The same procedure was applied to patients affected by glaucoma and retinal vascular diseases.

**Results:** The scotopic and photopic OPs presented a general amplitude reduction after the ocular hypertension induction, but the scotopic OPs only revealed statistical differences ($P<0,05$ criterium) between the amplitudes before and after the suction applied. After OP normalization, An evident and rapid recovery appeared with a trend to a relative hypervoltage. The raletion between OPs and IOP was not directly linear but the amplitude presented a "plateau" before +40 mm Hg, probably due to the protection effect of the retinal autoregulation, followed by a rapid decrease. The latencies did not show important variation. The OPs evolution presented features when the test was administred to the pathological subjects.

**Conclusions:** The flash ERG seem to be an useful method for studing the retinal autoregulation in condition of circulatory stress both in normal and pathological conditions.

## EOG and ROD-ERGs DURING DARK-ADAPTATION

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**Introduction:** Retinal dark-adaptation after a long-time light exposure is partially mediated by retinal pigment epithelium. Its course has an effect upon the variation of the corneo-retinal dipole characteristics. The aim of this work was to compare the variation of the amplitude and implicit time of the corneo-retinal potential during dark-adaptation by recording on the one hand EOG and on the other hand rod-ERGs.

**Methods:** EOG and rod-ERGs were recorded in 10 normal subjects, EOG according to international procedures and rod-ERGs by using 10 short wavelength stimuli delivered on a scotopic background during a 20-minute-dark-adaptation.

**Results:** EOG minimal amplitude (dark trough) and rod-ERGs maximal amplitudes were recorded after an 8-minute-dark-adaptation. Both signals showed a 30% amplitude variation.

**Conclusions:** The similarity of the time course and amplitude of these two different corneo-retinal dipoles suggest that they are mediated by parallel processes during dark-adaptation. These results are of special interest as far as rod-ERGs are recordable with or without subject's cooperation in most circumstances. Their recordings may give indirect information about the retinal pigment epithelium functionning in children, in non cooperative elderly or in animals on which EOG are not recordable.

## NEW SCLERO-CONJONCTIVAL ELECTRODES AND CONTENTION DEVICE FOR CLINICAL ERGRECORDINGS ON DOG AND CAT

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**Introduction:** The aim of this work was to provide a constant uniform retinal illumination during ERGs recordings on dog by providing a good head immobility, an adjustable stimulus position and an electrode fixation device. This device allowed us to avoid artifacts and provide a constant retinal illumination during ERGs recordings on dog and cat by providing a good globe fixity and keep the eyelids open.

**Methods:** Ten healthy anesthetized beagle dogs (20 eyes) and 10 healthy anesthetized european cats (20 eyes), previously adapted to a photopic background (30 cdm-2) for at least 3 hours were assessed. Normal retinal functioning was checked by recording ERGs elicited by achromatic flashes successively under a photopic background and a scotopic one. ERGs were recorded for each eye with an active sterilizable U curved copper clip retractable in its sheath (impedance 3 KW, diameter 0.2 mm) placed at the junction between the sclera and the bulbar conjonctiva. The reference electrode consisted of a single use needle electrode placed at the junction of the ear lobe and the temple. The ground electrod was placed in the interscapular area.

**Results:** Conjonctivitis happened in one dog and disappeared after 24 hours. ERGs were discernible from background for all stimulation and all tested animals. They show a classical morphology with « a » and « b » wave. They were symetrical for all animals.

**Conclusions:** These electrodes allows a perfect immobility of the globe during the whole recording whatever the duration of the exam. They were perfectly tolerated. This technic is very feasible and gives reproducible Results: This technique can be used as well as for clinical investigation than for toxicological one's.

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## ERG C-WAVE IN C57BL/10 MICE WITH A NEGATIVE ERG AND A LOSS OF BIPOLAR CELL SYNAPSES

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**Introduction:** In a subset of C57BL/10 mice (male and female) a preferential loss of the scotopic ERG b-wave ("negative ERG") associated with a loss of bipolar cell synapses can be observed (C57BL/10-minus). The aim of this study was to establish a reliable method for recording the ERG-c-wave in mice and to elucidate pigment epithelial function in C57BL/10-minus.

**Methods:** The ERG c-wave was recorded in 9 six-month-old C57BL/10-minus and 7 littermates without ERG abnormalities. After 2 hours of dark adaptation the animals were anesthetized by ketamine and xylazine. Corneal contact lens electrodes were used as active, silver needle electrodes as reference and ground electrodes. A red LED placed in front of the eye delivered a 250 ms stimulus at 3 intensities well above b-wave threshold. The lower cut-off frequency of the amplifier (Toennies, Hoechberg, Germany) was set to 0.08 Hz, the recording time was 5 seconds.

**Results:** In both groups of mice the ERG c-wave could be reliably recorded. Amplitudes and implicit times grow with increasing stimulus intensities. Although c-wave amplitudes of the control mice (305 - 421 μV) tend to be higher than those of the affected (274 - 372 μV), the difference was not significant (ANOVA, $p = 0.23$). In contrast, the c-wave implicit time of controls was significantly longer (1134 ms - 1322 ms) than in affected littermates (1015 - 1216 ms).

**Conclusions:** Using a low frequency amplifier and a stable configuration of the active electrode reliable recordings of the ERG c-wave in mice are possible. In a subset of C57BL/10 mice in which a selective reduction of the ERG b-wave amplitude associated with a loss of photoreceptor-bipolar cell synapses was observed (C57BL/10-minus) the c-wave seems to be only mildly attenuated. As the c-wave consists of two components - the corneal negative slow PIII generated by Mźller cells and the positive deflection mainly due to the hyperpolarization of the RPE apical membrane - both structures seem to be functional in these mice. In addition, the common trigger for both c-wave generators, the light-evoked decrease in extracellular potassium occurring in the subretinal space, must also be present in mice with the abnormal photoreceptor-bipolar cell synapses. Like the negative ERG this is again an indication for functional photoreceptors in C57BL/10-minus.

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# TOPOGRAPHIC MAPPING OF THE RETINA BY USING A SCANNING LASER OPHTHALMOSCOPE EVOKED MULTIFOCAL-ERG (SLO-M-ERG)

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**Introduction:** Mapping of retinal function in the central visual field by using a confocal scanning laser ophthalmoscope evoked multifocal-ERG (SLO-m-ERG).

**Methods:** A confocal scanning laser ophthalmoscope is used as a stimulator and trigger unit to perform a multifocal-ERG. The stimulus matrix of 19 to 241 hexagonal elements is covers a visual field of 14°. The visual stimulus is generated by a helium-neon laser (632,8 nm) with a power range of 0-200 µW. Illumination by another infrared laser (780 nm) permits simultaneous fundusscopy and control of fixation. is given by using an infrared laser (780 nm) with a power range of 0-2000 µW. The posterior pole of the eye and the hexagonal matrix are visualised on a video screen. The frame rate is 50 Hz. To record the m-ERG a Jet-electrode, which allows clear observation of the fundus during the examination, is used. The amplitudes were slightly smaller when the m-ERG was recorded with gold-foil electrodes. The SLO stimulation technique gives the possibility of obtaining an m-ERG to carrying out the test without dilatation of the pupils.

**Results:** The software configuration allows measurement of provides the possibility to measure the amplitude density of the first and second order response (first order and second order Wiener kernel). Examinations in patients with impaired retinal function due to lesions on the posterior pole show reduction of amplitude in the first and second order component. The amplitude density can be measured in any given hexagon. It is also possible to get averaged values of areas with the same eccentricity (rings) or of definite sections. The fixation cross can be moved within the display so that in cases of eccentric fixation, the fovea always lies at the centre of the display. Impaired retinal function can also be measured in patients with eccentric fixation by eccentric positioning of the fixation cross in this way, that the fovea is centred to the central hexagonal field. First results are have been obtained in patients with macular dystrophies, age related macular degeneration, macular holes (Gass II-III), diabetes, glaucoma, inflammatory retinal disorders and patients with retinal dysfunction without visible morphologic alterations.

**Conclusions:** The m-ERG evoked by a scanning laser ophthalmoscope evoked m-ERG offers a new method of topographic mapping of retinal function under permanent control of fixation. Since the examined test field covers only the central 14° the SLO m-ERG is especially suitable to examine patients with retinal disorders of the posterior pole of the eye. For the first time we are able to directly correlate an electrophysiological response to the individual topography of the retina visualised and recorded with the SLO technique.

## THE STUDY OF PATTERN VISUAL EVOKED POTENTIALS IN PATIENTS WITH DYSTHYROID OPTIC NEUROPATHY

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**Introduction:** The aim of our study was evaluation of pattern visual evoked potentials ( pVEP) in diagnosis and monitoring of dysthyroid optic neuropathy ( DON).

**Methods:** We tested pVEP in 54 patients with Graves' ophthalmopathy (GO) , including 8 patients with clinical signs of dysthyroid optic neuropathy ( DON) and 51 normal subjecst served as controls. We examined the amplitude (A), differences between amplitudes (DA) , latency (L) at P100 and N75 waves. In 30 patients with GO we recorded changes in pVEP before and immediately after treatment ( systemic steroids and radiotherapy).

**Results:** The mean latency at P100 (110,6 +14,4ms) and the mean latency at N75 ( 80,7 + 10,4ms) were significantly longer in 30 patients before treatment than in control group($p<0,05$). In 12/30 (39%) patients we observed prolongation of L P100 , in 10/30 (33%) patients - of LN75. After treatment the mean latency of both waves was significantly shorter compared to values recorded before therapy ($p<0,05$). The LP100 was still prolongated in 5/30(17%), the LN75 in 10 / 30(33%) treated patients compared to the control group. There were no significantly differences in the mean AP100 , AN75 and DA in patients before and after treatment. In patients with DON the LP100 was 125,2 + 17,4 ms, the L N75 - 93,3 + 19,8ms. Thry were significantly longer compared to patients without DON and the A and DA were significantly smaller in this group in comparison to control group. In patients with DON the clinical results of treatment were much worse than in patients without DON.

**Conclusions:** Pattern VEP is a sensitive mrthod of detecting early involvement of optic nerve in patients with GO. It reveals even asymptomatic nerve dysfunctions. The most important factor in diagnosis of DON is the latency at P100 and N75.The LP100 is the most useful data in monitoring the treatment of DON - it is significantly shorter after therapy. The amplitudes and differences of amplitudes are less useful - they demonstrated large intraindividual differences in all group. The diagnosis of optic nerve dysfunction by pVEP enables early and thus more effective treatment.

## FUNDUS CONTROLLED MULTIFOCAL ERG RECORDING USING A CONFOCAL MULTI-WAVELENGTH SCANNING LASER SYSTEM

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**Introduction:** To facilitate fundus-controlled multifocal ERG recording by choice of green and blue as stimulus colours, application of response-optimized stimulus patterns, and registration by non-corneal electrodes.

**Methods:** The Heidelberg Retina Angiograph ("HRA", a confocal scanning laser ophthalmoscope, Heidelberg Engineering) is modified for pixelwise triggering of its argon laser by a pattern stimulation and measurement device (RETIscan, Roland Consult, "RR"). The latter is coupled to the electrooptic modulator of the HRA laser unit (argon green = 514 nm or argon blue = 488 nm). Following Sutters principle, a pattern of hexagonal stimuli is generated. To increase individual responses, comparably few hexagons (19) are used to cover the whole stimulated area. M-sequences are displayed and the first order kernels are recorded. Stimuli, fixation and fundus are continuously monitored, the fundus being visualized by an an infrared laser (830 nm). Corneal (ERG-Jet), conjunctival (Gore-tex fibers) and skin electrodes (gold-cup) were applied. During a feasibility study, some laboratory modifications were attached to the system: to reduce stimulus intensity but not the fundus monitoring IR radiation, a cut-off filter (Zeiss F 60) was placed in front of the optics exit.To prevent straylight responses of the more pericentral retina, stimulation area overall diameter was increased up to 30 degrees so as to fill in the optics exit as far as possible, and the optics exit was surrounded by a white, ring-shaped adapting field covering the region of 15 to 40 degrees of excentricity.

**Results:** In healthy volunteers, multifocal ERG amplitudes as obtained by the RR + HRA system display their maximum centrally, levelling off with increasing eccentricity. The region of the blind spot can be identified by low or even non-recordable ERG activity. Responses picked up by non-corneal electrodes follow a similar pattern, their amplitudes being, however, reduced to about one half or one third, respectively, of those recorded corneally.

**Conclusions:** The combined Roland Retiscan RR and Heidelberg HRA devices appear suited to record multifocal ERG responses even by non-corneal electrodes. Maintenance of a clear retinal image is essential for multifocal ERG recording and this is alleviated by non-corneal electrodes. Limitations regarding the resolution and maximal number of hexagons need to be addressed in further studies. Some system modifications realized at a laboratory level still need to be implemented into the customized version of the apparatus. A continuous adapting illumination exceeding the stimulated area in visual angle would be particularly useful.

## ERG RECORDINGS TO CONE ISOLATING STIMULI IN PATIENTS WITH RETINAL DEGENERATIONS

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**Introduction:** To study the dynamics of the long- (L-) and middle-wavelength-sensitive (M-) cones in patients with retinal degenerations, we measured ERG response thresholds to stimuli, which modulate the two cone types in a predefined manner.

**Methods:** We tested normal trichromats and patients with retinitis pigmentosa (RP) and Best's disease. The diagnosis was based on a full clinical evaluation including standard electroretinography. The stimuli (30 Hz flicker and 66 cd/m2 mean luminance precluding rod input) were presented on a computer controlled monitor. The excitation in each cone type by the monitor phosphors was calculated from the phosphor emission spectra and the cone fundamentals. We measured the thresholds to stimuli which modulated exclusively the L- or the M-cones or the two in various combinations (both in phase and in counterphase). S-cones were not modulated.

**Results:** In the normal subjects the responses to pure L-cone modulation were about 40 degrees delayed relative to the M-cone responses and the tresholds to in phase modulation of L- and M-cones were smaller than those to counterphase modulation. Patients with Best's disease showed subnormal thresholds (supranormal amplitudes) in our ERG recordings for all combinations of L- and M-cone modulation. The temporal characteristics of the ERG response were within normal limits. RP patients showed generally larger thresholds for nearly all conditions. L-cone response phase in RP patients were delayed by about 150 degrees compared with the M-cone response phase. The M-cone response phase was within normal limits, but the L-cone response phase was delayed compared with those of the normals. RP patients showed smaller thresholds to counterphase modulation than to in phase modulation of L- and M-cones. This can be explained by the extreme phase differences between L- and M-cone responses in these patients.

**Conclusions:** We conclude that ERG recordings to cone isolating stimuli are potentially useful to characterize the pathophysiology of retinal degenerations. L-cone dynamics are altered in RP patients, whereas M-cone dynamics seem to be normal. Cone dynamics are not changed in patients with Best's disease. ERG amplitudes are smaller in RP patients and larger in patients with Best's disease when compared with normals. The extreme phase differences between L- and M-cone responses in RP patients remain to be explained.

## ETHANOL AFFECTS THE PHOTORECEPTOR - PIGMENT EPITHELIUM INTERACTION

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**Introduction:** The retinal pigment epithelium (RPE) provides support for the neuronal photoreceptors. Thus the RPE-photoreceptor interaction resembles a glia-neuron relationship in several ways. RPE cells respond electrically to a drop in extracellular potassium ([K+]o) induced by a cessation of the dark current in photoreceptors during illumination, resulting in an increase of the transepithelial potential (TEP). From clinical studies in humans it is known that instillation of Alcohol (Ethanol) increases ERG b-wave and c-wave amplitudes and causes a slow oscillation of the RPE standing potential (=TEP). We employed an in vitro RPE-retina preparation of the chick to evaluate effects of ethanol on the RPE-photoreceptor interaction.

**Methods:** Freshly dissected retinae with adjacent RPE and choroid were transferred to an Ussing-type perfusion chamber and ERG c-waves were elicited by repetitive short light pulses (4 sec) for 8 to 14 hours. ERG, direct-current standing potential (TEP), transretinal potential (TRP), and [K+]o were recorded intraretinally by double-barrelled, K+-sensitive microelectrodes. Ethanol and drugs could be applied to either retinal or RPE-basal side of the preparation by separate perfusion systems.

**Results:** (1) Ethanol induced a damped fast oscillation (((3 min), consisting of a trough followed by a peak, and a damped slow oscillation of the TEP which resembles a decrease to a minimum at about 25 min These responses were dose dependent over a range from 0.2% to 1.0%. When retinal perfusion was switched back to control medium the ethanol off-response closely matched the on-response in time course and amplitude but was of opposite sign. (2) In contrast, if ethanol was added to the RPE-basal side, no effects on RPE's electrical properties were detected. (3) When K+-channels were blocked by 2 mM $BaCl_2$ the positive going wave of the fast oscillation of the ethanol on-response as well as the negative going wave of the fast oscillation of the off-response were greatly enhanced, revealing actions of ethanol which were not dependent on [K+]o. (4) Ethanol decreased the amplitude of the light-induced change of [K+]o in the outer segment layer and therefore reduced [K+]o-dependent responses of the RPE (c-wave) and the slow PIII which is generated by Müller cells. Since the negative going slow PIII was suppressed, the fast cornea positive b-wave of the Müller cells was increased.

**Conclusions:** Data from the in vitro chick preparation suggest that ethanol has multiple effects on the electrical properties of the RPE, most probably by a modulation of transport mechanisms at the RPE- apical membrane. Ethanol's effect on the ERG b-wave and c-wave, however, seems to be due to a direct action on the photoreceptors resulting in a reduction in [K+]o amplitude at the outer segments and, as a consequence, a rather complex change in ERG components.

# ANALYSIS OF RETINAL FUNCTION IN ANIMALS USING MULTIFOCAL ERG WITH SCANNING LASER OPHTHALMOCOPE (SLO) STIMULATION

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**Introduction:** To determine the applicability of multifocal electroretinography using SLO stimulation in normal animals and models for retinal diseases.

**Methods:** Due to the photopic condititons, we have selected animals with sufficient cone function, such as rabbits, cats, and chicken. Animals were examined with a PC-based multifocal ERG system (Roland Consult, Germany) using a resolution of 19 to 37 hexagonal elements. The stimulus was generated by a SLO system using a green (514 nm) Laser for stimulation and an infrared Laser for simultaneous fundus control (Heidelberg Engineering, Germany). The stimulation frequency was reduced by inserting a blank frame after each pattern to reduce adaptation effects. Peak amplitudes and implicit times of first order kernels were determined for all elements for correlation with retinal morphology.

**Results:** So far, we have examined rabbits and chicken. In rabbits, the visual streak of high cone content resulted in high amplitudes, and the adjacent area covered with myelinated nerve fibers from the optic nerve head gave low amplitudes. This result could be replicated at different positions of the stimulus. In chicken, the topography of responses is difficult to judge because of their avascular retina and the almost equally distributed receptors. However, as one of the chicken was stimulated after being euthanized at the end of the experiments, the bleaching of the receptors by the hexagonal stimulus was observable since the pigment could not be regenerated any more. The usefulness of the multifocal technique in conjunction with a SLO in retinal degenerations is currently tested in a cat model.

**Conclusions:** These preliminary results show for the first time the feasibility to obtain local ERGs in animals with a green laser SLO stimulator in conjunction with a multifocal ERG system. Due to the spectral sensitivity of most retinae, some of which do not even contain receptors for longer wave-lengths, stimulation with a green laser can be expected to be superior to a red laser in terms of ERG amplitudes.

# VISUAL EVOKED POTENTIAL AND THE LOCALIZATION OF THE SOURCES OF BIOELECTRICAL ACTIVITY

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**Introduction:** There is no doubt about the significant role of visual evoked cortical potentials (VECP) in the diagnostics of the level of visual system injury. The topographic mapping of VECP has expand its diagnostic possibilities owing to development of computer technique. The new stage in analysis of VECP is localization of the sources of bioelectrical activity and their comparison with computer tomography and brain topography.

**Method:** We offered the method of localization of sources of bioelectrical brain activity, appearing to different light stimuli, such as achromatic and color reversal, motion - onset patterns and others. The construction of maps of distributing VECP on the surface of the scalp, localization of sources of activity was realized by means of personal computer program Brainloc (firm MBN, Russia). The program is intended for definition and tracking centers of electric excitements presented in the volume of the brain produced in one- or two-equivalent dipole sources (EDS). The parameters of EDS, three-dimensional (3-D) coordinates in brain volume as well as vector moments characterizing the intensity and orientation of sources, were defined in the consequence decisions of inverse problem by means of consecutive change of the dipole model parameters with the purpose of minimization of the sum of squares deviation of the calculated potentials on the surface of the scalp from simultaneously measured values of VECP. The search of the minimum of the sum of squares deviations was carried out by combined algorithms of minimization with limitations. The region of the change of 3-D coordinates of dipole sources at search of the minimum was confined to ellipsoid surface, which approximated the surface of the brain. There were investigated 12 healthy subjects at the age of from 20 till 40 years. 16-points recording by international system 10-20 Jasper were used as entering information simultaneous values. The degree of authenticity of the localization of sources was taken into account and inauthentic data was estimated as the presence of broader zone of processing information.

**Results:** Differences in the localization of sources in the right and the left hemispheres were detected at the stimulation of the right and left eyes separately. The highest activity for N-85 wave flash VECP was defined in tectum, mesencephalon, cerebellum. For P-100 wave the source was detected in upper lip of calcarine sulcus, cuneus, parietal occipital sulcus at first in contralateral hemisphere and then in ipsilateral one, for N-135 wave in thalamus, frontal - parietal lobe. The VECP sources in reversal pattern of N-85 wave were localized in parietal-occipital and hippocampus region close to the cortex surface. For N-100 wave the source was revealed in occipital region at the level of cuneus, posterior horn and in parietal-occipital region between corpus collosum and hippocampus. For N-135 wave it was in the ipsilateral occipital lobe.

**Conclusions:** The localization of VECP sources may be used in the investigations of various channels of visual system, because it allows to trace the way of spreading bioelectrical activity in the brain structures during the processing of visual information and at the recording of VECP of different modality in the dynamics evolution of wave complexes. Program Brainloc allows to determine the level of disappeared, conserved and increased bioelectrical activity at pathological processes in visual systems and levels of disturbance of visual information processing.

# SPECTRAL AND TEMPORAL ATTRIBUTES OF THE COLOR PROCESSING MECHANISM IN THE HUMAN RETINA REVEALED BY MULTISPECTRAL HARMONIC STIMULATION (FIS)

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**Introduction:** The human ERG, recorded under photopic conditions using the Fourier Interferometric Stimulation (FIS) is analysed to reveale the color processing in the retina. Earlier investigations demonstrated, that the color opponent mechanisms in human color processing can directly be shown by using colored FIS stimuli and analyzing the phase- and amplitude-spectra of the response from the eye. For more detailed specification of the involved processing steps the linear and nonlinear components of the retinal reaction are investigated for different stimulus frequency bands. Comparing the resulting phase and amplitude spectra for several stimuli series and different stimuli frequencies we gain information about the spectral and temporal attributes of the different underlying color processing mechanisms.

**Methods:** The output of a Xenon light source is modulated in time and spectral composition by an Michelson interferometer. The resulting FIS stimulus if spectrally filtered to stimulate only a subset of the human receptors. The FIS stimulus consists of all spectral components. Each wavelength is modulated in intensity by a certain frequency . The range of the intensity modulation frequencies is close to an octave for the wavelegth the human eye is sensitiv to. By changing the speed of the mirror in the Michelson interferometer this frequency range can be shifted. We were recording 5 series of measurements by doubling this frequency band each time, starting from 1-2Hz up to 16-32 Hz. The light is projected into an Ulbricht sphere for "Ganzfeld" stimulation. The ERG reaction is recorded using an eye cup electrode (Nicolet). The "white" light of the Xenon light source is modified by colored glasses: one which attenuates green, a second which attenuates blue and red, a third which is yellow and a fourth which is deep red.

**Results:** A measurement series consists of 5 times doubling the frequency band for each of the color filters.The responses for each measurement series at diffferent speeds and filter differ enormously. By increasing the stimulus frequencies an increase of the phase lag can be observed. This leads directly to the temporal response characteristics of the underlying color processing mechanism. The differences in response amplitudes give information about the flicker characteristics, especially the time properties of the color opponent mechanism. The comparison of the different measurement series gives information about the relation of input of the different cone types into the blue-yellow and red-green color opponent channels.

**Conclusions:** Seperate stimulation of the color opponent channels is possible with the FIS stimulus and specific broad band color filters. From a complete set of measurements the time transfer properties and color opponent mechanisms can be identified.

## THE IMPORTANCE OF ELECTROPHYSIOLOGICAL EXAMINATIONS IN THE DIAGNOSIS OF PARKINSON'S DISEASE

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**Introduction:** The dopamine depletion of the patients with Parkinson's disease influences also the electrical activity of retina. The aim of this paper is to judge the contribution of the EOG an ERG methods used in the diagnosing of the Parkinson's disease.

**Methods:** The observed group of 20 persons with extrapyramidal syndrome passed an EOG and ERG examination. To the patients was then applied apomorphine and the EOG and ERG was repeated. The improvement of the extrapyramidal syndrome was also evaluated by using the neurological scale.

**Results:** The reduction of the EOF rate as well as of the amplitude of the b-wave in scotopic ERG was found in all persons of the study group during the first examination. After the application of apomorphine the amplitude of the b-wave increased as well as the EOG ratio. The authors compare the importance of electrophysiological methods and neurological tests in the diagnosis of Parkinson's disease.

## EVALUATION OF MACULAR FUNCTION AFTER LASER TREATMENT OF SOFT DRUSEN

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**Introduction:** To evaluate benefits and risks on macular function of laser treatment of soft drusen in age-related macular degeneration.

**Methods:** In a prospective, controlled study,19 patients with soft confluent drusen involving the fovea were treated with krypton laser photocoagulation.Visual acuity, color photography, fluorescein angiography and electrofunctional tests(perg, vep on-off at spatial frequency(sf)of 1.16,2.32 and 9.32 c/d)were performed before treatment and after 1,6 and 12 months.

**Results:** The treated eyes showed a significant reduction of drusen during the follow-up.visual acuity and perg remained unchanged.contrast sensitivity threshold at sf of 1.16 c/d showed a reduction(statistically significant at t-test of student($p<0.002$)) at the first month in treated eyes, recovering the previous values after six months and after one year.

**Conclusions:** Laser treatment is able to lead to soft drusen resolution without impairment of macular function.

## "FLASH-ERG IN CHOROIDAL MELANOMA: AN UP-REGULATION OF bFGF?"

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**Introduction:** To define possible factors involved in the reduction of the b-wave of flash-ERG in patients affected by choroidal melanoma.

**Methods:** I.S.C.E.V. standard flash-ERG were recorded from both affected and control eye on 27 patients before surgical operation (local excision or enucleation). The choroidal melanomatous mass ranged from 4 to 20 mm in extension. Specimens of tissue from both melanomatous retina-choroid complex and unaffected areas were taken from 5 enucleated eyes to measure the level of bFGF mRNA, utilizing the technique of semiquantitative reverse trascription-polymerase chain reaction (RT-PCR).

**Results:** All 27 affected eyes showed a marked b-wave reduction with respect to the fellow eyes. In 5 specimens the expression of bFGF mRNA showed an increase in lesion free specimens with respect to melanomatous mass.

**Conclusions:** ERG changes similar to those observed in eyes affected by melanoma have also been recorded in the presence of bFGF upregulation in animal model (Stone J, Cervetto L, Gargini C and Bisti S: Optic nerve section suppresses the b-wave of the electroretinogram. Invest Ophthalm Vis Sci 38, S1122, 1997). We suggest that the melanoma triggers a process leading to an upregulation of bFGF in the human eye.

## MOTION ONSET EPs UPON BLIND HALF-FIELD STIMULATION

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**Introduction:** The motion-onset response in adults to short lasting motion and long lasting interstimulus intervals consists of a PN waveform, of which the positive component (peak latency around 120 ms) has a striate origin and the negative component (peak latency around 170 ms) an extrastriate origin. This extrastriate component is mainly found in the same hemisphere irrespective whether the left or right visual half field is stimulated.

**Question:** Are these two components generated sequentially or in parallel?

**Methods:** To answer this question, motion-onset VEPs to half field stimulation were recorded from a hemianopic patient.

**Results:** Stimulation of either half-field yielded a motion negativity but the response upon stimulation of the blind half-field had a longer latency and smaller amplitude. Furthermore, this response disappeared at low contrast whereas the response from the seeing half-field is contrast-invariant.

**Conclusions:** Since the hemianopic patient studied had a lesion in the left striate cortex, the motion negativity with prolonged latency upon right half-field stimulation cannot be generated by means of the geniculate striate pathway. A likely alternative is generation by means of the superior colliculus, and if so, this pathway needs higher contrasts than the striate pathway to yield motion onset EPs. (Supported by the Copernicus program).

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## VISUAL EVOKED POTENTIALS ELICITED BY MOVING STIMULI: CAN WE EXPECT TO FIND A UNIQUE MOTION-VEP?

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**Introduction:** To record visual evoked potentials (VEPs) elicited by moving stimuli in normal human subjects as a means of testing the visual motion sensitive, magnocellular channel.

**Methods:** Three motion paradigms (motion onset; motion reversal; motion coherence) were used; the moving stimuli were unidimensional and two-dimensional noise stimuli. Different spatial and temporal parameters of the stimuli were used (i.e. contrast, spatial frequency, speed, duty cycle,...). The possible influence of different electrode montages was evaluated.

**Results:** Although it is very well possible to record VEPs using moving stimuli, it is clear that the interindividual variability within the same motion paradigm can be large. Strict stimulusparameter control can partially explain this variability. Multiple stimulusparameters and their interaction dictate the precise waveform, ranging from a predominant positivity to an exclusive negativity. This diversity probably also correlates with the large number of cortical areas activated during visual motion perception.

**Conclusions:** We strongly advocate further research before a standard method for recording motion-VEPs can be proposed.

# ANALYSIS OF THE ELECTRICAL EXCITABILITY OF THE CHICKEN RETINAL NETWORK BY MEANS OF A PLANAR MICROELECTRODE ARRAY

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**Introduction:** Several visual prostheses for restoring vision to patients with retinal degeneration are being developed currently [1,2,3]. They aim at restoring vision by focal electrostimulation of retinal neurons. In the subretinal approach images are to be fed into the visual pathway by electrical excitation of the neuronal network by a subretinally implanted microphotodiode array [4]. To test how the retinal network responds to local electrical stimulation and how subretinally applied spatial voltage patterns are encoded, we used a recently established in-vitro method for electri-cal stimulation of retina preparations and recording of evoked slow potentials and ganglion cell activity by means of microelectrodes [5,6].

**Methods:** Retina segments were prepared from newly hatched chicken and adhered either with the receptor or the ganglion cell side to a microelectrode array (MEA, [7] ) with 60 substrate integrated planar electrodes (Au or TiN, O 10 µm, spacing 100 µm and 200 µm, respectively). In both configurations sclera and retinal pigment epithelium were removed. With the ganglion cell side down a needle microelectrode was positioned onto the receptor layer to apply monopolar current pulses. Evoked slow potentials and ganglion cell activity were recorded extracellularly from the MEA-electrode located below the stimulation site (bandwidth 0.1 Hz-20 kHz). With the receptor side down stimulation was done by applying voltage pulses via selected MEA-electrodes to the distal ret-ina. Spike activity evoked by these spatial stimulus patterns was recorded extracellularly from ganglion cells by means of a patch electrode. To produce evidence of network excitation, modulators of synaptic transmission (GABA, AP4, Kynurenic acid, 100µM; Mg++ 6mM) were added to the bath solution.

**Slow potentials.** Recordings of field potentials revealed complex stimulus-correlated signals that are highly correlated with ganglion cell activity. The most prominent feature, a large nega-tive going wave, could be elicited either by positive or negative pulses depending on the intraretinal location of the stimulating needle electrode. Variation of pulse duration and strength modulates the temporal and spatial pattern of field potentials and spike activity.

**Spike activity.** Application of different spatial voltage patterns via the MEA-electrodes resulted in distinguishable temporal patterns of individual ganglion cell activity. Spike patterns consisted of early bursts, transient inhibition or delayed discharge. They depend on the spatial configuration of the stimuli (points, bars, edges), distance between stimulating and recording site and pulse strength. With blocked synaptic transmission ganglion cell responses and slow potentials were altered or disappeared.

**Conclusions:** Our in vitro assemblies are well suited to study central points related to a subretinal prosthesis. Requirements to elicit spatial and temporal distinguishable slow potentials and ganglion cell activity can be evaluated simply in vitro. From the viewpoint of functional electrical stimulation our results are transferable to in vivo.

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## LUMINANCE DISTORTION PRODUCT MAY AFFECT VEP ACUITY ESTIMATES IN HUMAN INFANTS

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**Introduction:** MacLeod and He (1993) reported that on-off gratings of very high spatial frequency can produce whole-field flicker even though the time-average luminance is constant. The cause of the flicker is probably a time-varying distortion product created at an early non-linearity. They could null the perceived flicker by adding spatially uniform, temporal luminance modulation of the appropriate amplitude and phase. The same effect could in principle occur when VEP acuity is measured in human infants. We asked whether the infant VEP at high spatial frequencies is the result of flicker caused by such a distortion product.

**Methods:** High-contrast, on-off square-wave gratings were presented to 1- to 8-month-old infants. In order to determine the VEP acuity, the steady-state VEP was first recorded for a 10-second spatial-frequency sweep. A spatial frequency just below the estimated acuity was chosen for the next test phase. With spatial frequency fixed at this value, temporal luminance modulation was added, increasing from 0 to 20 cd/m2 over the 10-second sweep. The phase of the modulation was varied from one sweep to another.

**Results:** In some infants, the luminance modulation had little if any effect on the VEP; this suggests that their VEPs reflect response to the grating, not to a distortion product. In other infants, however, luminance modulation at a specific phase and amplitude caused a significant decrease in the VEP response; this suggests that their VEPs reflect response to a distortion product.

**Conclusions:** The VEP to on-off gratings may be contaminated in some infants by response to a distortion product. In such cases, the VEP may over-estimate visual acuity.

## ELECTRICAL STIMULATION THRESHOLDS IN NORMAL VERSUS DEGENERATE (RD) MOUSE RETINA

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**Introduction:** To study the effect of varying stimulation parameters on the excitation threshold in normal and diseased retinas in order to identify the safest and most efficient stimulation paradigms for the development of a retinal prosthesis.

**Methods:** Retinal ganglion cell and optic nerve recording were obtained from anesthetized normal sighted (C57BJ) and rd (C3H) mice in response to an electrical stimulus delivered to the retinal surface by a platinum electrode. Excitation thresholds were measured for electrical stimulation using biphasic square wave, sinusoidal and pulse train stimulus waveforms.

**Results:** The excitation thresholds for a biphasic square wave pulse in the normal retina was significantly lower than that of the disease retina. Both latency and chronaxie were significantly longer in the normal mouse than in the rd mouse. Stimulation with pulse train longer than the chronaxie resulted in higher excitation thresholds than stimulation with single pulses.

**Conclusions:** Despite a near total loss of photoreceptors, controlled electrical stimulation of the rd mouse inner retina results in a recordable neural response from surviving retinal ganglion cells. A pulse train shorter than the chronaxie appears to be the safest, most efficient stimulus. The lower excitation threshold, longer latency and longer chronaxie in the normal mouse implies that the photoreceptor is the site of stimulation while the bipolar cell appears to be the probable site in the rd mouse.

## CLINICAL AND RETINO-CORTICAL CONDUCTION ALTERATIONS IN PATIENTS AFFECTED BY CLASSICAL CONGENITAL MUSCULAR DYSTROPHY ( Cl-CMD ) ASSOCIATED WITH MEROSIN DEFICIENCY

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**Introduction:** The immunocytochemical analysis of laminin a-2 (merosin) chain in the muscles of patients with Classical Congenital Muscular Dystrophy differentiales the types of the disease associated with a deficit of merosin from those merosine positive. Patients with Central Nervous System involvement in merosin negative Cl-CMD always present alterations of the white matter at RMI, usually without clinical significance. While ocular malformations and damage to the Central Nervous System are described in some subtypes of CMD ( Muscle Eye Brain Disease, Walker Warburg Syndrome ), ocular involvement and retino cortical conduction in merosin negative Cl-CMD are not well known.

**Methods:** This study reports about five patients affected by merosine negative Cl-CMD. All the patients presented important alterations of the white matter associated with ventricular enlargment and, in one case, with pachigyria. Refraction, visual acuity, ocular motility, the anterior segment and fundus were examined. ERG maximal, cone and rod response, Transient Pattern Reversal Visual Evoked Responses were carried out as well.

**Results and Conclusions:** Significant alterations at the standard ophtalmological examination or of the electroretinographical response were not registered, while in three cases important modifications in the retino cortical conduction ( reduction in wideness associated with low visual acuity, increase in latency, reduction in amplitude of the lateral derivations ) were observed. This demonstrates an involvement of the optic pathway at different levels in this disease.

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## ELECTROPHYSIOLOGY USING THE SCANNING LASER OPHTHALMOSCOPE

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**Introduction:** The scanning laser ophthalmoscope (SLO) has some useful features for electrophysiology. One essential feature is the possibility to image the fundus with either visible or infrared lasers. Therefore, the position and stability of the fixation can be controlled during the entire data aquisition which is useful especially for methods which permit spatial resolution like multifocal ERGs. An acousto optic modulator in the beampath of the laser allows temporal and spatial modulation of the laser intensity, so that the position, intensity and duration of the stimulation can be exactly controlled.

**Methods:** A SLO (Rodenstock, München) was used to test different Methods: The HeNe laser (633 nm) was used for stimulation. Multifocal ERG: The originally monitor-based multifocal ERG system RETISCAN (Roland Consult, Wiesbaden) was adapted to the SLO. It is essential that the entire data aquisition is synchronize by the SLO. Sweep VEP: A pattern generating software (OPHTAPATTERN, Rodenstock) allows the presentation of a fast sequence of checkerboard patterns of different spatial frequency (e.g. 0.5, 1, 2, 5, 10 cycles per degree). Long-duration light stimuli: Using a purpose-written software, long-duration stimuli (e.g. 160 ms, spatially homogenous) can be used to stimulate photopic electroretinograms. The responses were recorded using the EMS system (taberna pro medicum, Lüneburg), which was modified to be triggered externally.

**Results:** Multifocal ERG: The simultaneous observation of the fundus image and the position of the stimulating hexagons allows an exact assignment of the measured responses to the retinal location, even for patients with eccentric fixation. The amplitude peaks at the foveal center and decreases with increasing eccentricity. Furthermore, the multifocal SLO-ERG allows the function of retinal implants to be tested. Sweep VEP: The VEP amplitude as a function of checksize shows a behaviour similar to that of monitor based systems with the advantage of an exact control of the position and the focus of the stimuli during testing. Long-duration light stimuli: Long-duration light stimuli allow the separation of on- and off-responses (d-wave) of the photopic electroretinogram. Using stimuli with 160 ms duration, the d-wave can be clearly detected.

**Conclusions:** The SLO is a useful instrument for some special electrophysiologically examinations. One of the main advantages is the control of fixation. Furthermore, the results can be compared to other SLO-based methods with high spatial resolution like fundus perimetry, autofluorescence and retinal densitometry. Further improvements should include the use of additional laser wavelengths.

## SIMULTANEOUS RECORDING OF PVEP AND EYE-HAND REACTION TIME IN AMBLYOPIA: ARE DIFFERENCES MOVEMENT RELATED?

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**Introduction:** The purpose of this study was to further characterize the functional differences between strabismic amblyopia (SA) and anisometropic amblyopia (AA).

**Methods:** Simultaneously recordings of full-field monocular and binocular PVEPs and eye-hand reaction times (average of 100 responses) were obtained from 11 normal subjects and 10 amblyopes of a similar age range. The stimuli consisted in the reversal of black/white checks (1-2 sec. random intervals) of 0.3, 2 and 8cpd and 3% and 93% contrast. For each condition (3 sizes X 2 contrasts, 2 monocular and 1 binocular) the peak time of the P1 wave of the PVEP was compared to mean RT evoked to the same stimulus.

**Results:** Irrespective of the stimulating conditions, the binocular PVEP and RT responses of AA and SA did not seem to be affected by the delayed visual pathways; both method showing a suppression effect. Similarly, SA and AA could not be distinguished on the basis of the monocular PVEP responses irrespective of the stimulating parameters; both forms of amblyopia yielding equivalent delays from the amblyopic eye. In contrast while in normal subjects there were no significant differences in RT obtained between preferred and non-preferred eye, amblyopic subjects showed a significant difference in RT between their two eyes. In AA, this difference was seen with the 8 cpd, 93% contrast (mean interocular difference: 116.76ms) and 0,4cpd, 3% contrast stimuli (mean interocular difference: 31.93ms) where as in SA only the 8cpd, 93% contrast stimuli resulted in a significant interocular RT difference (mean: 91.55ms). No such differences could be evidenced with the PVEP measurements.

**Conclusions:** Our results suggest that compared to the PVEP, the RT is a better method to distinguish the two forms of amblyopia. Our results are slightly different from those previously reported by this laboratory (McKerral et al., ARVO 1997) where the RT was triggered by appearance of a central target. The above discrepancy might reflect the "pseudo-movement" which results from the reversal of the checkerboard stimuli, a feature of the stimulus which would be enhanced (as acknowledged by the subjects) with the RT measurements. More research combining the RT procedure with movement stimuli should confirm this initial impression. Supported by MRC (PL) and FCAR (PL & FL).

## ELECTRORETINOGRAPHIC FINDINGS IN PATIENTS WITH CRX MUTATIONS

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**Introduction:** The cone-rod homeobox (CRX) gene is a retinal transcription factor mapping onto chromosome 19q13.3. Mutations in the CRX gene were recently reported in patients with autosomal-dominant cone-rod degeneration. We have identified 3 families in which CRX mutations appear to cause retinal degeneration.

**Methods:** To date we have conducted clinical and electrophysiological studies in two of these families. Standard full-field ERGs and rod intensity response functions were obtained from affected members. Inaddition, high intensity flashes were used to elicit rod and cone a-waves over a series of retinal illuminance. Computational models of the leading edge of the a-wave were used to analyze transduction parameters for both rods and cones.

**Results:** Family A has an Ala177-Thr (missense) mutation. The proband was tested initially at the age of 54 years and has been followed for 13 years. The standard ERG protocol showed a typical pattern of cone-rod degeneration. Rod and cone amplitudes have decreased linearly over time (adj. R2 0.9, $p<0.02$; ~3% amplitude loss/year for rods and ~6% amplitude loss/year for cones). For the rods, both gain of phototransduction (log S) and b-wave sensitivity (log k) were close to normal. For the cones, the a-wave analysis revealed a 1 log unit reduction in the gain parameter. Family B had an Ala196+1bp (insertion/truncation) mutation. The proband was a 30 year old female who showed a typical pattern of cone-rod degeneration on standard ERG testing. Rod b-wave sensitivity and photoreceptor gain were normal. Cone phototransduction was abnormal with a decrease in gain 0.7 log unit. The father, age 54, had a 30 Hz flicker amplitude <1 microV, while retaining a sizable rod response with normal gain of phototransduction. Family C has a Leu146del13 (deletion/truncation) mutation of the CRX gene, leading to severe retinal degeneration at an early age

**Conclusions:** Mutations of the CRX gene cause a progressive form of cone-rod degeneration, inherited dominantly. Patients show greater loss of cone than rod responses and in patients tested to date, the phototransduction parameter (log S) is normal in rods, but substantially reduced in cones. Despite these phenotypic similarities there are, nevertheless, differences among families that may be due to the specific mutation within the CRX gene.

## MAGNOCELLUAR DEFICITS ARE HIGHLY CORRELATED IN EYE AND BRAIN IN BOTH DYSLEXIA AND GLAUCOMA

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**Introduction:** Large cells are thought to damaged first in glaucoma. In some cases of dyslexia too psychophysical, electrophysiological and anatomical evidence suggests the magnocellular system functions poorly. The differences in contrast gain of the magnocellular and parvocellular systems are so marked that contrast is the stimulus feature which best isolates responses from the two systems. If low contrast (about 20%) is combined with coarse pattern (about 0.25cy/deg) and rapid alternation (about 7Hz) the resuting responses is very specific for the magnocellular system. Similarly, high contrast (about 100%), fine (about 4cy/deg). slowly alternating (about 2Hz) patterns are optimal for the parvocellular system.

**Introduction:** To correlate contrast thresholds for magnocellular system specific stimuli in cortex and retina, usng VERs and PERGs respectively, in early glaucoma suspects and dyslexics and to contrast this with their parvocellular responses.

**Method:** The dyslexics were children whose reading age was 2 or more years behind mental age on the Neale Test. Glaucoma patients and high risk suspects were diagnosed independently by the referring ophthalmologist . Magnocellular function was isolated with 50,30,20,10 and 5% contrast bars of 0.25cy/° (VERs) or 0.125cy/° (PERGs) reversing every 70msec. Parvocellular function was isolated with VERs and PERGs to 1, 4 and 8 cy/°, 100% contrast bars reversing every 330msec or PERGs to 1 octave coarser bars reversing every 210msec. Flash VERs and Focal ERGs were recorded as controls. A parvocelluar response was considered normal if it was clear at 8cy/deg and there was no delay at 1cy/deg. The lowest contrast at which a clear dominant response at the stimulating frequency could be detected was taken as the contrast threshold. The thresholds in each eye (R or L) of each group were analysed seperately.

**Results:** We established that all patients had normal parvocellular responses. PERGs had a higher contrast threshold and less steep contrast gain function. Patients showed variable losses to the coarse rapidly alternating patterns. The PERG and VER contrast thresholds were always highly correlated in both eyes of both groups. In a few eyes, where one of the two responses were normal and the other was abnormal, both tests were equally likely to be abnormal. There were many instances of strong familial associations in the dyslexia data including a pair of identical twins, both with unrecordable responses. Glaucoma suspects varied from being normal to having 30msec phase delays and normal PERGs. Only diagnosed early glaucoma cases had absent responses in both tests.

**Conclusions:** Responses from both cell populations can be recorded independently and are correlated throughout the visual pathway. Reduced magnocellular function originates in the retina in both dyslexia and glaucoma. Magnocellular losses, identifying a simple anatomical problem, are marked in some dyslexics. A graded degree of loss occurs so early in uncertain glaucoma cases that it has the potential to facilitate management.

## EXPERIENCES WITH "TOMEY PE 400" PORTABLE ELECTRODIAGNOSTIC EQUIPMENT

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Authors have a two years period of experience with TOMEY PE 400 in clinical practice. The equipment is compact and easy to operate and suitable for measuring ERG /flash, pattern and flicker/ and VEP /flash and pattern/. Unfortunately it is not available for EOG. The technique and results of the examination processes will be presented.

## USE OF SIMULTANEOUS RECORDING OF PATTERN ELECTRORETINOGRAM AND VISUAL EVOKED POTENTIALS TO DIFFERENTIATE PAPILLITIS FROM ANTERIOR ISCHEMIC OPTIC NEUROPATHY

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Pattern evoked responses and pattern electroretinogram have been recorded in 32 patients with unilateral papillitis and in 30 with non arteritic anterior ischemic optic neuropathy.In group of papillitis there were 12 patients with definite multiple sclerosis.

Simultaneous pattern visual evoked potential and results of pattern electroretinogram were recorded.The pattern reversal stimulation was obtained with aid of Medelec television pattern regenerator.Visual acuity in all patients was better than 0,1. In anterior ischemic optic neuropathy (AION), the P100 of PVEP was delayed in 26 eyes (Ave. 118,73msec;normal 106,9msec) , ($p<0,05$).In group with papilitis in all 32 eyes the prolongation of the latency P-100 was noted (Ave.135,63 msec) ($p<0,001$).One of the most striking differences between AION and papilitis PVEP response was seen when the normal eye was stimulated. In patients with AION the PVEP response was always normal, while in patients with unilateral papillitis in 15 patients was abnormal. The group with anterior ischemic optic neuropathy had significantly reduced amplitude P-100 ( ave.4,1mV ; normal 8,7mV ), and amplitude/latency ratio( ave. 0,031 mV/msec.; normal 0,082mV/msec) , compared with group with papillitis ( $p < 0,01$).

The P50 and N95 components of the pattern electroretinogram were also analyzed. Analysis of the PERGs in group with AION showed abnormally reduced amplitude of N95 peak, and middle decrease in patients with papillitis.In both group, with papillitis and AION , the mean values of P 50 amplitude was normal.

These results support opinions that the P50 an N95 components of the pattern electroretinogram have different retinal origin.

We concluded that PVEP and PERG provides a useful diagnostic and monitoring tool in patients with papillitis and anterior ischaemic optic neuropathy.

# THE PATHOLGICAL PROCESSES VISION IN THE CLINICAL ELECTROPHYSIOLOGY

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The problem of a vision and uninvasive localization of the pathological process in the clinical electrophysiology and practical medicine is extremely important.

It is known methods and device of the pathological processes detection and localization: roentgenodiagnostics, fibrigasteroscopy, computer tomography, ultrasonic diagnostics et cetera. One of them, for example, roentgenodiagnostics, are connected to adverse effect of the short-wave electromagnetic radiation. Other: fibrigasteroscopy, - with painful feelings; ultrasonic diagnostics - with adverse effects on the attendants; computer tomography - with a deficit of devices and dearness of procedures. These methods is informatve in that case, when in tissues and organs exist appropriate morphological changes. The purpose of given research is uninvasive fast painless detection and localization of the pathological process by the electrophysiological procedure. The biophysical substantation of a offered method consists in following. If in a bodys persons some horizontal section to create (with the help two electrodes) a high-frequency electrical current, its size at a given voltage will depend on a tissues general impedance of this section. For similar environment the distribution of fall of potential is linear. But as the sections tissue is not homogeneous environment, the tissues impedance in this section will vary depending on those bodyes, which are in this section, and the linear distribution will change. Isopotentials, belonging to given section, leave on a bodys surface, so the measurement of a electrical fields parameters in given section inside a body can be replaced by measurement of potentials on a persons leather. The pathological centers occurrence changes a picture of isopotentials distribution and force lines in section. The necrotic natures pathological process is expressed in reduction of conductivity (in increase of a impedance) biotissue. Distortion earlier a symmetric picture of fields (distribution of the isopotentials and force lines) is thus found out. The inflammatory natures pathological process , on the contrary, is expressed in a increase of conductivity (reduction of a impedance) biotissue. Distortion of a initial picture is thus also found out. However, this change of isopotentials distribution and force lines has other character. On the basis of distortions availability of the imaging picture of a electrical field (including by force line and isopotentials) device, enabling to find out and location pathological process in organism is created. This device for impedance-visualization of a pathological processes site contains: high-frequency alternating currents power, voltmeter, two electrodes to power, third electrod to voltmeter. The device works as follows. One powers electrode is established stationary in a point on horizontal section with prospective pathological nidus. Second electrode is moved on the surface of a body in researched section. Thus on each step mobile electrode from the voltmeter a point with half-significance of a set voltage is defined. If this point lies in a geometrical centre between two powers electrodes, pathology or is in this point, or is away between two powers electrode. The choice between these two variants can be executed, having made mobile opposite electrode. Given device for impedance-vision of a pathological processes site is protected by the patent of Russia.

## VECP AND COLOUR VISION TESTING IN CHILDREN WITH HYDROCEPHALUS

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**Introduction:** Headache, vomiting and papilloedema are the key symptoms of increased acute brain pressure. In patients with chronic increased brain pressure various neurological and ophthalmological symptoms are observed. The aim of the study was the determination of the damage of the visual system caused by chronic increased brain pressure.

**Method:** 28 children in the age from 3 to 18 (mean 8,5 years) were examined. 26 patients were operated and had a ventriculo-peritoneal shunt. None of the patients was examined in the acute stage of the disease. All patients received a full ophthalmological and neurological status, most of them a Arden colour vision test; in all visual evoked potentials were recorded (1 Hz, 30 min of arc, 70 cd/m2 ). 30 age-matched normal children served as a control group.

**Result:** 14 patients did not receive a re-operation of the shunt, while the others had had between one and nine re-operations. The operation was performed between half a year and 12 years before the examination. 18 children had a spina bifida. Major neurological deficits were only observed in these patients. The visual acuity ranged from 0.6 and 1.2 (mean 0.9). Strabismn was observed in 14 of the patients. A double-peak was observed in 12 patients (43%), broadened amplitudes in 16 patients (56%). The latencies of the first P-100 peak did not significantly differ from the control group. Only in one child of the control group a double-peak and broadened responses were seen. Normal colour vision was seen in 27 patients, while one boy demonstrated a inherited red/green deficiency.

**Conclusions:** The chronic increased brain pressure lead to a deficit of the visual system which is represented by the high incidence of strabismn as well as the pathological VECP responses represented by the broadened amplitude and the double peak.

## ERG RESPONSE TYPES DEVELOP AT DIFFERENT RATES

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**Introduction:** The purpose of this study was to determine how different ERG response types in the normal human electroretinogram (ERG) change with subject age. This has been an ongoing study (preliminary data presented at ISCEV 1994)

**Methods:** Subjects were 60 children, 10 days to 15 years old, and 30 subjects 15-37 years old. ). Since our earlier study we have redefined our subject group. We excluded patients with optic nerve disease, neurological impairment or with a known family history of genetic eye disease. Thirty-four children had nystagmus (57%), which subsequent to electrophysiological and clinic exam was attributed to idiopathic congenital motor nystagmus. The remainder were volunteer subjects, or subjects referred for photophobia or eyestrain. ERGs were recorded using the standard protocol established by the International Society for Clinical Electrophysiology of Vision, with Burian-Allen bipolar contact-lens electrodes. We measured rod response, maximal response, oscillatory potentials (OPs), cone response, flicker response, and b-wave amplitude/log intensity (V/log I) curve. Growth curves derived from the Naka Rushton equation gave measures of rate of growth and time to reach half the adult amplitude. We compared subjects grouped by sex, and use versus no use of sedation during testing.

**Results:** Dark- and light-adapted ERG a- and b-wave amplitudes reached adult levels by three to five years of age. In early infancy OPs were the most immature of the ERG response types, although the rate of development thereafter exceeded that of the other response types such that OP amplitudes were within adult levels by two years of age. Amplitudes of the ERG responses in 21 children sedated with chloral hydrate did not differ significantly from those of 23 who had not been sedated.

**Conclusions:** ERG response types develop at varying rates, reflecting different developmental stages in photoreceptors, middle retinal layers, and more proximal retina.

## THE OBJECTIVE EVALUATION OF THE INTERACTION BETWEEN COLOR VISION AND MOTION PERCEPTION

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**Introduction:** To measure equiluminance values of green/red grating luminosity ratios with different moving velocity in normal subjects and to explore the interaction between color vision and motion perception.

**Methods:** Optokinetic nystegmus (OKN) of eye movements elicited by moving color grating stimulus could be recorded with electrooculograph (EOG). The equiluminance points were determined when OKN changed in direction in various moving velocities. Sixteen cases (32 eyes) normal subjects were tested, 6 cases male and 10 cases female, Age ranged from 20 to 51 years old.

**Results :** The mean equiluminance points were 0.525 , 0.425, 0.397, 0.391, 0.367 under 595, 400, 301, 239 and 200 mm/s groups of grating moving velocity respectively. There were statistically significant differences of mean equiluminance points among 595mm/s group and other groups($P<0.01$), there were no statistically significant differences of mean equiluminance points among other 4 groups (P0.05).

**Conclusions:** The human color vision is influenced by the motion when moving velocities increased to a certiain degree.

# THE INFLUENCE OF $MgCl_2$ ON THE LIGHT-INDUCED POTASSIUM INCREASES AND THE ERG b-WAVE OF THE ISOLATED SUPERFUSED RCS RAT RETINA

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**Introduction:** The purpose was to determine whether second order neurons of the retina of the Royal College of Surgeon (RCS) rat are still functional immediately after the photoreceptors have spontaneously degenerated; and whether the result indicates which cells contribute to the ERG b-wave.

**Methods:** Experiments were done on isolated superfused RCS rat retinas in which the photoreceptors degenerate spontaneously. The electroretinogram was recorded, and light-induced potassium increases in the distal and proximal retina were measured with double-barrelled potassium-sensitive microelectrodes (Corning 477317) during superfusion with a physiological solution with and without 10mM MgCl2.

**Results:** As with other breeds of rats, in RCS rats between 19 and 24 days postnatal the distal potassium increase (0.09±0.02mM, n=8) is enlarged by MgCl2 (0.16±0.04mM, n=8), but the proximal potassium increase (0.23±0.11mM, n=10) is slightly decreased under the influence of MgCl2 (0.20±0.15mM, n=10). In RCS rats 29-35 days postnatal the distal (0.10±0.03mM, n=10) and proximal potassium increases (0.14±0.05mM, n=9) are still recordable, but are reduced under 10mM MgCl2 (distal 0.01±0.03mM, n=10; proximal 0.03±0.04mM, n=9). In all instances MgCl2 abolished the b-wave.

**Conclusions:** At about the 33rd postnatal day the photoreceptors of RCS rats are severely damaged and the potassium decrease around photoreceptors is then no more measurable. The potassium increases, which indicate the continuing function of second order neurons, are however still present. Our conclusion is that the initial degeneration is confined to the photoreceptors and for a while, at least, the second order neurons are still active. The potassium increases are dependent upon the integrity of ionotropic (e.g. off-bipolar, AII-amacrine, horizontal cells), and metabotropic synapses (on-bipolar cells). MgCl2 blocks only ionotropic synapses. In the younger RCS rat the enlarged potassium increase under MgCl2 in the distal retina occuring in parallel with the loss of the b-wave indicates that on-bipolar cells contribute to the b-wave. The reduced potassium increase in the proximal retina when MgCl2 is applied indicates that AII-amacrine cells may also contribute to the b-wave generation.

## CONE ERG AMPLITUDE GROWTH WITH LIGHT ADAPTATION IN PATIENTS WITH RETINITIS PIGMENTOSA

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**Introduction:** To study growth in amplitude of cone electroretinogram to white flash stimuli during light adaptation in retinitis pigmentosa.

**Methods:** 50 patients with typical retinitis pigmentosa (RP) aged 13 to 81 years and 23 normal controls aged 14 to 62 years were examined. Cone ERGs were recorded to 5 Hz full-field white flash stimuli in the presence of a bright white background illumination (50 cd/m2), over a period of 20 min.

**Results:** Cone ERG b-wave amplitudes at baseline ranged from 0.54-57.5 microvolt in RP, and 45.0-125.0 microvolt in normals. Cone ERG b-wave implicit times ranged from 26.0-50.8 msec in RP, and 25.0-28.2 msec in normals. Amplitude growth during light adaptation ranged from 27-99% of baseline amplitude in normals. 49 RP patients showed an amplitude increase (8-174%), and one patient showed a decrease of 7%. The amplitude growth was below the normal range in 17 patients, and it was above the normal range in only one patient whose baseline amplitude was 12 microvolt. The mean for cone ERG amplitude growth in RP was 42% (SD 29%) and 51% (SD 19%) in normals, and no significant difference was observed between two groups. Changes of b-wave implicit time during light adaptation ranged from -4.2 msec to +3.8 msec in RP, and were not significantly different from those in normal controls (from -1.2 msec to +1.4 msec).

**Conclusions:** Cone ERG amplitude growth during light adaptation is not exaggerated in RP patients, but within or below the normal range, irrespective of the baseline amplitude in this method.

## RELATION BETWEEN VEF AND VEP - REPRODUCIBILITY AND RELIABILITY

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**Introduction:** There were many papers in which VEF(visually evoked neuromagnetic field) elicited from SQUID (Superconducting Quantum Interference Device) was more accurate than VEP(visually evoked potentials). However, both of them are thought to be produced from the same current dipole which is generated in the brain by stimulus. Therefore, VEF and VEP must behave similarly. Little difference exists between the conducting speed in the brain of electric and magnetic potential. Very little is known about VEF by contemporary researchers despite its recent increase in popularity. To clarify the relationship between VEF and VEP, we investigated the difference in the position of the current dipole by each method from the same stimulus.

**Methods:** VEF are elicited from Neuromag-122 and VEP are elicited from Brain atlas (Biologic Co. Ltd.). Stimulus patterns are projected on screen paper by a video-projector. Horizontal and vertical bar patterns and a checkerboard pattern were utilized as stimulus patterns. VEF data and VEP data are averaged from 100 sets of data. The dipole created by VEF and VEP respectively is calculated for each machine.

**Results:** As for latency, reproducibility in VEF is relatively good and is similar with that of VEP. As for the position of the dipole, VEF is more widely distributed than VEP. The topography of VEF must be interpreted by a combination of positive and negative peaks, however that of VEP may not necessarily be interpreted by combination in this way. The position of the dipole in the case of VEP is under the peak.

**Conclusions:** In conclusion, as neither can provide perfect results on their own, both VEF and VEP should be utilized together in order to provide a more precise position of a dipole activated by a stimulus.

## SPATIAL SELECTIVITY OF BINOCULAR INTERACTION OF ANISOMETROPIC AMBLYOPES STUDIED WITH DICHOPTIC VEP

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**Introduction:**The aim of the present study was to determine the spatial selectivity of binocular interaction with normal and defected binocular vision.

**Method:**Steady-state VEPs elicited by dichoptic reversal checkerboards with check sizes ranging from 10-120 min of arc were recorded on 30 normal subjects and 30 anisometropic amblyopes. The binocular interaction was measured as the Binocular/monocular VEP amplitude ratio(B/M) for the dominated eye or the normal eye of amblyopes.

**Results:**(1)In normal subjects,when each eye was stimulated by the same size,the B/M was minimum.The value of B/M increased as the check sizes of each eye were made progressively more unequal.(2)In cases of anisometropic amblyopia the B/M reached its minimum value when each eye was stimulated by the same size,but it was statistically significant larger than the normal.

**Conclusions:**Binocular interaction show spatial selectivity to pattern stimulus in normal subjects.It was most pronounced when the checkerboard sizes of the stimulus to each eye were identical and the interaction decreased with increasing difference between the sizes of both eyes.In patients with anisometropic amblyopia,the binocular interaction was obviously decreased or even disappeared,the ability of processing spatial information decreased either.

**Key words:** dichoptic steady-static VEP binocular interaction spatial selectivity anisometropic amblyopia

# A NEW METHOD OF SEPARATING THE OSCILLATORY POTENTIALS FROM ELECTRORETINOGRAM

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**Introduction:** to avoid a loss of all oscillatory potentials.

**Method:** Using computer signal-process technique we combined the extended wavelet analysis with Fourier Transform under different bandpasses for 60 normal eyes.

**Results:** 1.Five wavelets of oscillatory potentials could be distinguished. 2.The latency of OP1 was found 2-3ms earlier than that of A-wave. 3.The standard deviation and variation coefficient of OPs of this method were smaller than using Fourier Transform. 4. Choosing the high cutoff frequency of 210-270Hz, the standard deviation and variation coefficient of OPs were smaller than choosing that of 300Hz.

**Conclusions:** the wavelets of OPs can be separated better from ERG by combining the extended wavelet analysis with Fourier Transform.

## SECOND ORDER KERNEL RESPONSES OF MULTIFOCAL ERG RECORDED FROM NORMAL SUBJECTS

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**Introduction:** It has been reported that second order kernel response of multifocal electroretinogram (M-ERG) reflects the function of inner retinal layer. However, this response is in general to small to be easily applied to the clinical eye diseases. We recorded the second order kernel responses from normal subjects and studied the reproducibility of these responses.

**Methods:** M-ERGs were recorded using the VERIS III system (Tomey Co. Ltd.) from four normal subjects, and were analyzed by VERIS Science software program. The stimuli consisted of densely arranged arrays of 103 or 61 hexagonal elements. It took 4 or 8 minutes to obtain one M-ERG record, and 8 or 16 sessions were required to perform this record respectively. To make artificial scotoma in the normal subjects, a black circular paper was attached on the VERIS III CRT monitor at the upper temporal parafoveal region.

**Results:** The reproducibility of first order kernel response was better than that of second one. Even after combination of three M-ERGs each trace of second order kernel response was not clearly recognized. Second order kernel responses obtained from the artificial parafoveal scotoma showed noisy traces which were similar to those responses elicited from the actually stimulated hexagonal elements.

**Conclusions:** In the standard stimulus and recording condition, second order kernel responses of M-ERG recorded from normal subjects showed poor reproducibility, and were too small to understand what these responses reflect in the retina.

# THE CONTRAST CHARACTERISTIC OF THE PATTERN ELECTRORETINOGRAM (PERG) DEPENDS ON TEMPORAL FREQUENCY

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**Indroduction.** The pattern electroretinogram (PERG) amplitude is believed to be linearly related to contrast. In the context of analyzing the effects of media opacities on the PERG, we measured its contrast-amplitude function at various temporal frequencies.

**Methods:** PERGs were recorded in nine subjects with a checksize of 0.8 degrees and a mean luminance of 45 cd/m2. Experiment 1 covered 6 temporal frequencies (pattern onset/offset in a transient (4 Hz) condition and pattern reversal at 7, 10, 13, 16, 21 rev/s) at 3 contrast levels (25 percent, 50 percent and 100 percent). A second experiment covered only 2 frequencies (7 and 21 rev/s) but with 5 contrast levels from 25 to 100 percent, in a large field (27 degrees x32 degrees) and a perifoveal condition (central mask of 15 degrees diameter).

**Results of experiment 1:** At all temporal frequencies the amplitude of the PERG increases with contrast, but the shape of the contrast-amplitude function varies markedly: Under transient conditions and at 7 rev/s the PERG increases linearly with contrast, but this function displays a progressively positive curvature at higher frequencies. At 21 rev/s a reduction of the contrast from 100 percent to 50 percent reduces the amplitude to 1/5.

**Results of experiment 2:** Experiment 1 was replicated, the amplitude-contrast characteristic was found to be linear at 7 rev/s and smoothely accelerating at 21 rev/s; the same characteristics were found when stimulating the perifoveal area alone.

**Conclusions:** This dependency of the contrast characteristic on temporal frequency is contrary to what would be expected from a magno/parvo model. Further, this contrast dependency needs to be taken into account when designing stimuli for use in patients that may have media opacities.

## SURVEY OF COMPLICATIONS OF INDOCYANINE GREEN CHOROIDAL ANGIOGRAPHY AND FUNDUS FLUORESCEIN AINGIOGRAPHY IN 116 CASES

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**Introduction:** To evaluate the safety of indocyanine green for use in fundus angiography.

**Methods:** We surveyed the complications of 116 cases that examined with indocyanine green choroidal angiography (ICGCA) and fundus fluorescein angiography (FFA), and collected and analysed their responses through asking them in detail at the same time.

**Results:** In two patients (1.7%), the decision was made not to proceed with ICGCA after positive preangiographic testing. The two patients had been hospitalizing and had been treating eye diseases with large dosage of hormone. Six patients (5.2%) took place complications when they were examining FFA. The complications of FFA were lighter and did not afect the examinations of FFA.

**Conclusions:** A comparison of frequency of adverse reactions of indocyaning green with the previously reported frequency of such reactions to fluorescein sodium indicated that indocyanine green is as safe as fluorescein for use in angiography. But we must pay attention to adverse reactions of ICGCA when large dosage of hormone is used.

**Keywords:** Indocyanine Green Choroidal Angiography, Fundus Fluorescein Angiography Complications

# GANZFELD ERG-RESPONSE OF ON-OFF CONE PATHWAYS TO A LONG-FLASH COLOUR STIMULUS

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**Introduction:** Within the cone-system there are two main types of channels: on-path-ways, responding to light increment; and off-pathways, detecting decrement of light, which produce electrical responses to the onset and offset of the light stimulus, respec-tively. Using brief-flash stimuli of less than 50 ms the on- and off- responses (b and d wave) merge into one, called clinical photopic b-wave. Application of the long-flash stimuli of 200 ms allows to separate on-response ( b-wave ) from off-response ( d-wave). To receive on- and off-responses from each of the three types of cones with maximum spectral sensitivity of 419 nm (blue), 531 nm (green) and 558 nm (red) each cone type was stimulated with monochromatic long-flash stimuli of the wavelength with its maximum spectral sensitivity. To suppress the responses of the other cones, a steady background of mean 50 cd/m2 is essential. The aim of this study was to define the assessment criteria for on- and off-responses for S-, M-, and L-cones and to suggest the optimal parameters for the possible clinical application. Patients with inherited colour vision deficiencies and hereditary macular dystrophies were examined.

**Methods:** A four-channel LED Ganzfeld stimulator (CH-Electronics) was used to produce long-flash square-pulse stimuli of 200 ms duration, presented with 2,5 Hz. Four series were performed to obtain on- and off-responses for all three cone types. A series of red stimuli of 72; 240; 720 cd/m2 were presented on steady green background of 41,3 cd/m2 (log of ratio stimulus/background is 0,2; 0,8 and 1,2 ) with steady blue background of 39 cd/m2. One serie of green stimuli of 124, 413, 1240 cd/m2 were presented on steady red background of 72 cd/m2 (with log ratio of 0,4; 0,8 and 1,3), the other of the same intensity on steady orange background of 52 cd/m2 (with log ratio of 0,4, 0,8; 1,3), both with steady blue background of 39 cd/m2. A serie of blue stimuli of 11, 7, 39, 117 cd/m2 was presented on intense steady background of 520 cd/m2 to suppress rods, the maximum spectral sensitivity of those close to B-cones. ERG was recorded with gold-foil electrode. Two recordings were obtained per stimulus intensity, each consisting of 50 cycles. Between series the patients were allowed to rest a few seconds.

**Results:** Preliminary data procession of the control group shows that for the same stimulus/background ratio red cones produce significantly smaller d-waves than green cones. Blue cones produce significant d-waves by intensities more than 39 cd/m2. For all cone types b/d amplitude ratio was more than 1. The mean b-wave latencies for red and green cones were 33,6 ms, latencies for blue cones were significantly shorter parallel to the increase of stimulus intensity. Patients with colour vision deficiencies showed the amplitude reduction for the affected cone types. Colour-ERG-recordings of patients with maculopathies also showed amplitude reduction, correlating to cone topography.

**Conclusions:** The colour-ERG proved to be a helpful technique for objective examination of patients with inherited colour vision defects and maculopathies.

# ELECTRORETINOGRAPHY IN RETINAL DETACHMENT WITH PROLIFERATIVE VITREORETINOPATHY

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**Introduction:** The effectivity of surgical treatment of retinal detachment (RD) depends on the character of alterations in the retina and stage or kind of proliferative vitreoretinopathy (PVR). The ambiguity of pathological changes determines the complexity of prognosis of the postsurgical dynamics of visual functions. In this connection, electroretinography can assume particular significance for the detection of distinctive signs, that are possibly bound with the favorable or the unfavorable flow of reconstructive process.

**Methods:** Before the evaluation of the dynamic of retinal electrogenesis at surgical treatment of RD it was necessary to carry out the analytical investigation of specificity of bioelectric activity of the retina for different PVR in presurgical period. 35 patients were examined with PVR type A (PVRA), B (PVRB), C2 (PVRC2), C3 (PVRC3) and D1 (PVRD1). There were recorded ganz-field ERG, macular ERG (MERG) and flicker ERG (FERG) on the frequency of flashes 12, 32 and 40 Hz as to previously reported methodologies. The comparative analysis of ERG and low-frequency FERG was used for the estimation of extent of involvement into the pathologic process of glial Muller cells and second order neurons.

**Results:** The analysis of results allowed to identify the main distinctive signs of retinal electrogenesis at RD in the groups of patients with various stages of PVR. These signs consist in following: PVRA - is characterized by moderate oppression of "a" and "b" ERG-waves and by feebly marked reaction of low-frequency FERG. These data point mainly at the reduction of functional activity of photoreceptors and glial Muller cells. But they indicate weak alterations of neurons in inner nuclear layer. PVRB - belongs with expressed amplitudes decreasing (up to 17-26% of norm) of "a" and "b" ERG-waves and FERG on all frequencies at less pronounced reaction on the part of MERG and high-frequency FERG. As in PVRA stage, the function of Muller cells changes to a greater extent as compared with neuronal activity. PVRC2 - is characterized by the increase of heaviness of changes of all biopotentials, especially of MERG. PVRC3 - functional changes in second order neurons are progressively developed, which is accompanied by the serious decreasing of amplitude of low-frequency FERG. PVRD1 - besides the attributes, typical for PVRC3, one can see the progressive reduction of the amplitude of photopic ERG-components: the pronounced oppression of ERG "a"-wave and FERG on high frequencies of stimulation.

**Conclusions:** There was obtained the differential electro-physiological characteristic of the retina, which allowed to judge about topography of pathologic process at various stages of PVR. The results of this work became the basis for the further investigating of the dynamics of functional retinal activity in the restoration period after surgical treatment of RD.

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**Bold-face type** indicates first author.

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